A Dissertation on

TO DETERMINE THE ASSOCIATION OF RISK FACTORS IN TYPE 2 DIABETIC PATIENTS WITH DIABETIC MACULAR ISCHEMIA

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CERTIFICATE

This is to certify that the dissertation entitled **"TO DETERMINE THE ASSOCIATION OF RISK FACTORS IN TYPE 2 DIABETIC PATIENTS WITH DIABETIC MACULAR ISCHEMIA"** by the candidate **Dr.KAVITHA.M** under my supervision and guidance at STANLEY MEDICAL COLLEGE, CHENNAI. The thesis is submitted by the candidate in partial fulfillment of the requirements for the award of M.S. Degree in ophthalmology, course from June 2012 to April 2014 at the Stanley Medical College, Chennai.

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DECLARATION

I hereby declare that this dissertation entitled **"TO DETERMINE THE ASSOCIATION OF RISK FACTORS IN TYPE 2 DIABETIC PATIENTS WITH DIABETIC MACULAR ISCHEMIA"** is bonafide and genuine research work carried out by me under the guidance of **Prof.Dr.K.BASKER**, M.S., D.O., HOD, Department of Ophthalmology, Government Stanley Medical College and Hospital, Chennai – 600 001.

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ABSTRACT

AIM:-To determine the association of risk factors in type 2 diabetic patients with diabetic macular ischemia. Materials and methods:-A cross sectional study was performed on 100 diabetic patients attending the out patient department of ophthalmology, govt Stanley medical college,Chennai, during the period November 2012 to October 2013. Patients who filled the inclusion criteria were included in the study. Detailed history about systemic medical illness and ophthalmic history were elicited. Ophthalmic examination included V/A,refraction, slit lamp examination of the anterior segment, IOP and fundus examination. Diabetic retinopathy graded according to the abbreviated ETDRS severity scale. Fundus fluorescein angiography done and diabetic macular ischemia graded according to the criteria followed by bresnick et al. Systemic examination included BP recording, lab investigations FBS, PPBS, HbA1c, lipid profile,urine routine,ECG done. Significance of associations are analysed using chi square test and all the significant variables in univariate analysis were included in the multivariate analysis to calculate adjusted odds ratio for the individual factors. Results:- The association of diabetic macular ischemia with nephropathy and uncontrolled DM were found to be statistically significant (OR 4.5, 95% CI 1.8-11.0, P value .001); (OR 2.9, 95% CI 1.2-7.4, P value .02) respectively,the association of other variables age,gender,duration of DM, HTN, IHD, hyperlipidaemia were p value 0.912,0.500, 0.539, 0.554, 0.476, 0.201 respectively not found to be significant. 9/13 eyes (69.23%) in severe;13/22eyes (59.1%) in moderate; 1/6 eyes(16.7%) in mild diabetic macular ischemia showed decreased visual acuity. Conclusion:- In our study the most significant associated factor was nephropathy followed by uncontrolled diabetes and the other factors like duration of DM, HTN, IHD, hyperlipidaemia were not as significantly associated as nephropathy. Also we found that visual acuity is more affected in severe grades of diabetic macular ischemia and preserved in milder grades of diabetic macular ischemia.

Key words: diabetic macular ischemia, fundus fluorescein angiography, HbA1c, diabetes mellitus,hypertension, IHD, hyperlipidaemia, risk factors, visual acuity, odds ratio.

CONTENTS

PART – I

PART – II

ANNEXURE

ABBREVIATIONS

DM	:	Diabetes Mellitus
DMI	:	Diabetic Macular Ischemia
FAZ	:	Foveal Avascular Zone
DME	:	Diabetic Macular Edema
ETDRS	:	Early Treatment Diabetic Retinopathy Study
DR	:	Diabetic Retinopathy
HTN	:	Hypertension
IHD	:	Ischemic Heart Disease
DCCT	:	Diabetes Control and Clinical Trial
UKPDS	:	United Kingdom Prospective Diabetes Study
WESDR	:	Wisconsin Epidemiology Study of Diabetic Retinopathy
V/A	:	Visual Acuity
Hb	:	Haemoglobin
MI	:	Myocardial Infarction
HDL	:	High Density Lipoprotein
HLA	:	Human Leucocyte Antigen
RBC	:	Red Blood Cell
VEGF	:	Vascular endothelial Growth Factor
IRMA	:	Intra Retinal Microvascular Abnormalities
NPDR	:	Non Proliferative Diabetic Retinopathy
PDR	:	Proliferative Diabetic Retinopathy

NVD	:	Neovascularisation Disc
NVE	:	Neovascularisation Elsewhere
FFA	:	Fundus Fluorescein Angiography
FA	:	Fluorescein Angiography
h/o	:	History of
CCD	:	Charge Coupled Device
HbA1C	:	Glycosylated haemoglobin
ECG	:	Electrocardiogram
ADA	:	American Diabetes Association
JNC	:	Joint National Committee
BP	:	Blood Pressure
CRA	:	Central Retinal Artery
SPCA	:	Short Posterior Ciliary Artery
CRV	:	Central Retinal Vein
CRVO	:	Central Retinal Vein Occlusion
CI	:	Confidence Intervel

INTRODUCTION

Epidemiology:-

Blindness is one of the most dreaded complication of diabetes, but also preventable. Current statistics suggests that total no of diabetics are expected to rise to about 300 million cases by the year 2025. The development of diabetes leads to increased propensity for developing irreversible macrovascular and microvascular complications.

Diabetic retinopathy rarely develops within 5 years of the onset of diabetes or before puberty, but about 5% of type 2 diabetes patients present with diabetic retinopathy at the time of diagnosis. Diabetic retinopathy, a microangiopathy affecting the small blood vessels due to hyperglycemia, damage is caused by both microvascular leakage and microvascular occlusion.

Visual loss in diabetic retinopathy is mainly due to neovascularisation in type 1 diabetes and maculopathy in type 2 diabetes.

Diabetic maculopathy:-

Diabetic maculopathy (either ischemia or oedema) is more commonly seen in type 2, compared to type 1 diabetes. The two types of maculopathy are often comorbid. All individuals with diabetic retinopathy are at risk of maculopathy, including ischemic maculopathy. Approximately 14% of diabetics have maculopathy, most commonly macular oedema, which typically precedes ischemia if left untreated. One study reported 8% of eyes affected by retinopathy had some evidence of ischemic maculopathy.

Diabetic macular ischemia (DMI) remains an important cause of visual loss in diabetic retinopathy in large part due to the devastating and irreversible visual loss that it causes in a minority of cases, and it is characterized by the presence of Foveal Avascular Zone (FAZ) abnormalities.

Importance of diabetic macular ischemia:-

Diabetic macular ischemia is extremely difficult to detect without the use of fundus fluorescein angiography, and it is generally regarded as untreatable, unlike PDR and DME. DMI severity grading standards were first established in the Early Treatment Diabetic Retinopathy Study (ETDRS report no: 11).

Since then numerous studies have demonstrated the relationship between the DMI and the severity of the visual loss and decreased contrast sensitivity. Further more, most studies[2,4,10,13] have demonstrated the FAZ abnormalities in DR, retinal ischemia or retinal capillary perfusion studies in diabetic retinopathy, but only very few studies are there to demonstrate the relationship of diabetic macular ischemia and its systemic associations.

Since the visual loss in diabetic macular ischemia is profound and irreversible, it is necessary to determine the associated risk factors in DMI and to identify the individuals at greater risk as early as possible by aggressively targeting the risk factors and timely intervention to prevent further progression and to reduce the visual morbidity due to macular ischemia.

The purpose of this study is to determine the association of risk factors like hypertension, hyperlipidaemia, ischemic heart disease (IHD), nephropathy in diabetic macular ischemia, since these risk factors were found to have common association, known effects on DME and PDR, similar microangiopathy and ischemic pathology.

REVIEW OF LITERATURE

Arthur James Ballantyne, worked on the immense problem of diabetic retinopathy.

In the pre Christian era the honey urine described by susruta and referred to as “a melting down of the flesh and limbs to urine” by aretaeus of Cappadocia.

In 1921 in toroto, Frederick grant banting and Charles Herbert best discovered and isolated insulin, the active principle of the beta cell of the islet of langerhans.

Mylius (1937) found the AV ratio was often 2:4 instead of 2:3 in prodromal stage of diabetic retinopathy.

Retinal microaneurysms originally noted by Mackenzie and Nettleship (1877) and attention was initially drawn by Ballantyne and Lowenstein, isolated sign of diabetic retinopathy.

Retinal capillary non perfusion was 1st described by ashton in diabetic retina using Indian ink preparation(10).

- Bresnick GH, Condit R, Syrjala S, Palta M, Groo A, Korth K. Abnormalities of the foveal avascular zone in diabetic retinopathy. *Arch Ophthalmol* 1984;102:1286-93(4). The Study showed FAZ abnormalities

like undulations, FAZ irregularities and increased FAZ in diabetic retinopathy cases.

- D Shukla, Chandra Mohan Kolluru, J Singh, Rajesh K John, M Soman, B Gandhi, R Kim, N Perumalsamy Macular ischemia as a marker for nephropathy in diabetic retinopathy[1]. To determine whether diabetic macular ischemia is associated with ischemic heart disease (IHD), hyperlipidaemia, hypertension (HTN) and nephropathy.

- Mansour AM, Schachat A, Bodiford G, Haymond R. Foveal avascular zone in diabetes mellitus. *Retina* 1993;13:125-28[9]. Retinal capillary nonperfusion is associated with FAZ enlargement, which is positively correlated with the increasing severity of the retinopathy particularly PDR.

- Sim DA, Keane PA, Zarranz-Ventura J, Bunce CV, Fruttiger M, Patel PJ, Tufail A,Egan CA[6]. Predictive factors for the progression of diabetic macular ischemia. The rate of FAZ enlargement ranges from 5%-10% of baseline FAZ area per year in eyes with established ischemia. A greater macular ischemia grade was independently predictive for progression, and diabetic macular ischemia progression itself was predictive of the loss of visual function.

Only very few studies were in the literature about Diabetic macular ischemia, due to difficulty in diagnosing and there is no definite treatment

option. The definite sequence of evolution of the DMI are not well understood but the risk factors associated with DMI are likely those of diabetic retinopathy in general.

Histological studies [9,10] showed acellular capillaries in the areas of capillary non perfusion in diabetic retina, patches of acellular capillaries coalesce to occlude the terminal arteriole, clinically it correlates with non perfusion of macular capillaries, diagnosed by fundus fluorescein angiography.

RISK FACTORS

MODIFIABLE RISK FACTORS

1. Poor control of diabetes

Hyperglycemia is an important factor in the cascading events of microvascular complications due to diabetes.

Epidemiological studies showed that strict blood glucose control can prevent or delay but doesnot eliminate the risk of development or further progression of diabetic retinopathy (Meyer le et al 2008).

DCCT study [15] showed that intensive glycaemic control results in delaying the development of retinopathy by 76%, slowed down the progression of diabetic retinopathy by 54%, also reduced the risk of albuminuria by 54%.

The UKPDS[7] showed that intensive control of blood glucose results in 25% reduction of risk of any diabetic microvascular end point and 35% reduction in risk of microvascular complications for every one point decrease in HbA1c (eg.,8%-7%).

2. Hypertension

Diabetes and HTN mostly coexists, with a prevalence of 40-60% over the range of 45-75 years. It remains undiagnosed and under treated in the diabetic as well as in general population. Type 2 DM & HTN when associated, may accentuate the changes of diabetic retinopathy and also carries an increased risk of albuminuria and renal disease.

Inceased blood pressure has an effect on blood flow, resulted in the development and progression of retinopathy by damaging the retinal endothelial cells[6]. Diabetic and hypertensive patients showed decrease in macular perfusion, which can be explained by progressive capillary closure with decreased perfusion and increased resistance[24].

United kingdom prospective diabetes study (UKPDS)[8] was a multicentred, randomized trial study showed that tight control of blood pressure less than 140/80 mm Hg slowed down the progression of retinopathy by 34% and also reduced the risk of microvascular and macrovascular complications. The UKPDS showed that the incidence of the retinopathy was associated with systolic blood pressure, for each 10mm Hg decrease in mean systolic blood pressure, a 13% reduction was found for microvascular complications.

In **WESDR study**[11], a 10mm Hg rise in diastolic blood pressure was found to be associated with a 330% increased 4-year risk of developing macular oedema in those with type 1 diabetes and a 210% increased risk in those with type 2 diabetes.

Nørgaard *et al*[24] found that arterial hypertension per se is not associated with increased retinal changes, but it may worsen these changes in patients with clinically apparent nephropathy.

3. Proteinuria and nephropathy

Nephropathy leads to rheologic, lipid and platelet abnormalities results in accentuation of diabetic retinopathy changes. There are reports that patients with renal failure having maculopathy, that improves after dialysis or renal transplantation.

The gross proteinuria at baseline has been reported to be associated with 95% increased risk of developing in the WESDR study (Moss et al 1988). The risk of PDR was 4 times higher in patients with persistent microalbuminuria of 4 years.

4. Elevated Serum lipids

The early treatment diabetic retinopathy study (ETDRS) showed a positive correlation between serum lipids and hard exudates in the macula and decreased visual acuity in type 2 DM patients.

Also WESDR study reported that increased serum cholesterol results in increased incidence of retinal hard exudates formation, also increases the risk of atherosclerosis and IHD (chew EY et al.1996)[14], Klein BEK et al 1991-1998)[11].

Gupta et al reported that using lipid lowering agents like statins along with macular photocoagulation resulted in decrease in severity of macular oedema and hard exudates.

5. Anaemia

ETDRS reported that anaemia is an independent risk factor for high risk PDR, 5 times increase in severe DR in low Hb. Few studies reported that Anaemia has been associated with progression of diabetic retinopathy (Davis et al 1998) (Berman DH et al 1998).

6. Pregnancy

During pregnancy there are high levels of oestrogen which accelerates the changes of diabetic retinopathy. The risk of progression of DR is related to the severity of DR in the first trimester,adequacy of

treatment, duration of diabetes, metabolic control before pregnancy and the presence of coexisting HTN. DME if it develops in late pregnancy, no need to treat because it usually resolves after pregnancy.

7. Smoking

Results in hypoxia, carbon monoxide and platelet aggregation, associated with MI, peripheral vascular disorders. No association with DR incidence, but there is little evidence in the progression of retinopathy as described by (Muhlhauser l et al 1996)[38]., (Karamanas B et al 2005).

8. Alcohol

Results in decreased platelet adhesiveness, decreased fibrinogen and increased HDL levels. Doesn't increase risk, may have beneficial effect in type 1 DM patients.

NON- MODIFIABLE RISK FACTORS

1. Duration of diabetes

Most consistent relationship observed in persons with diabetes is the increase in the frequency and severity of diabetic retinopathy, roughly 50% of patients develop diabetic retinopathy after 10 years, 70% after 20 years and 90% after 30 years of onset of the disease. According to the estimates of caird et al the risk of blindness for a given duration of diabetes increases with the age of the patient at the time of diagnosis.

2. Sex

Incidence is more in females than males (4:3), no significant differences in prevalence or progression.

3. Genetic Factors

Transmitted as a recessive trait, without sex linkage.

Type 1 DM:- Majority have HLA-DR3/DR4 association, has no effect on risk of PDR,3-6% siblings; 8% of off springs of affected father are affected

Type 2 DM:- Strong genetic predisposition, no HLA association,40% of siblings and 30% of off springs are affected.

PATHOGENESIS OF DIABETIC RETINOPATHY

Chronic hyperglycemia is the basic cause for diabetic retinopathy.

- When blood sugar increases it is converted to sorbitol by aldose reductase and further oxidized to fructose by sorbitol dehydrogenase.

- The 2^{nd} reaction is slow, leads to intracellular sorbitol accumulation, there is oxidative stress due to free radical generation, accumulation of advanced glycation end products and excessive activation of several protein kinase c isoforms.
- Disruption of ion channel function is an important early feature.

Early microvascular changes before onset of diabetic retinopathy incudes

- **Thickening of basement membrane:-** due to non enzymatic glycation of proteins, metabolites of sorbitol pathway, altered basement membrane collagen. This together with endothelial cell damage, changes in RBC's, stickiness of platelets leads to microvascular occlusion.

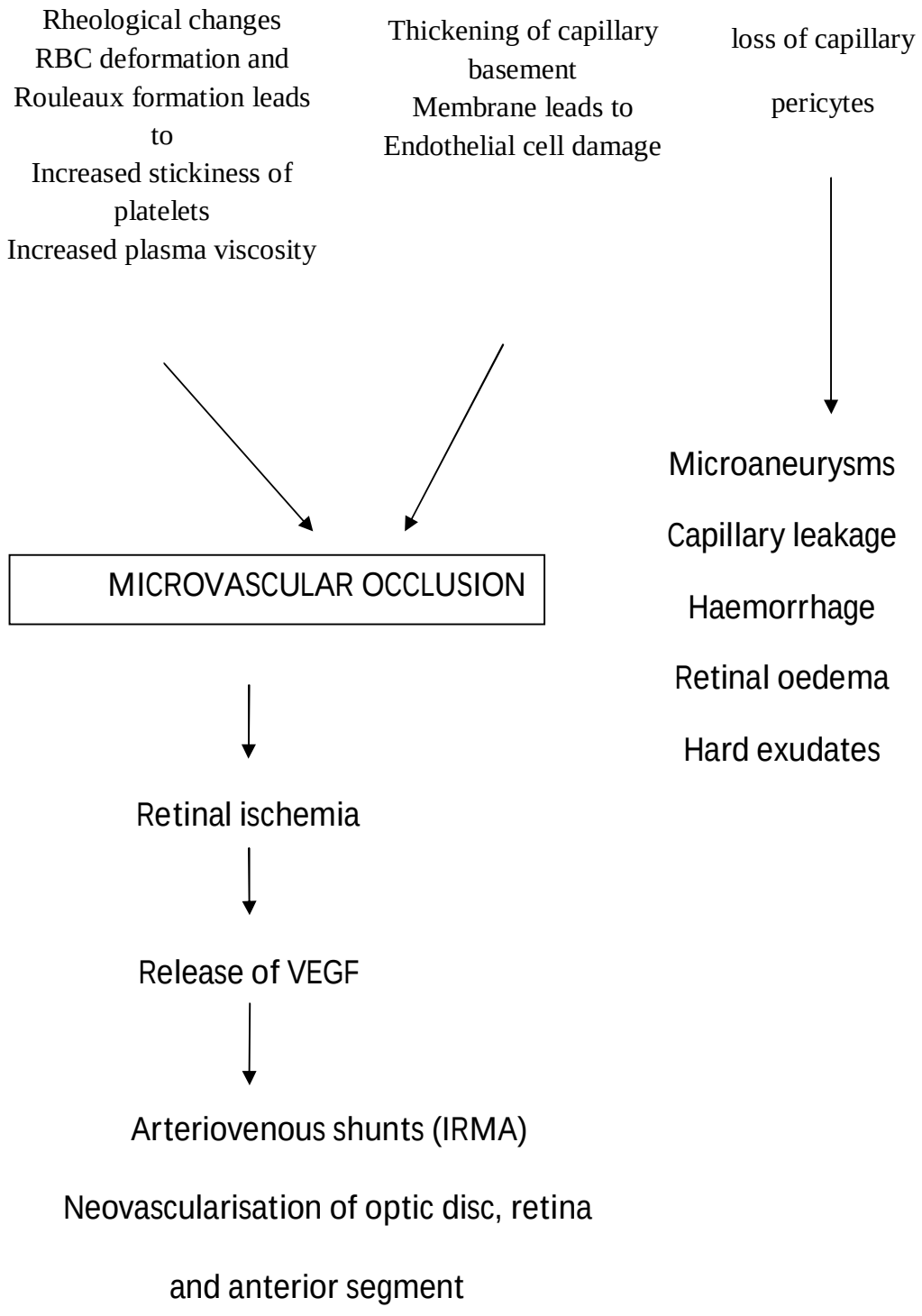
- **Loss of pericytes:-** selective presence of sorbitol pathway in pericytes responsible for early structural and functional loss.

The variety of fundus changes that occur in diabetic retinopathy is due to multiplicity pathologic abnormalities that may exist at all levels of the retinal vascular bed.

Retinal vascular changes in diabetic retinopathy at

- Capillary level present as – Microaneurysm, dilatation, abnormal Permeability and occlusion
- Arteriole level present as – narrowing of origin of terminal arterioles, Occlusion or sheathing
- Venular level present as – dilatation, beading, reduplication, looping, Kinking, branch/central vein occlusion

Vascular and haematological changes seen in diabetes mellitus



OPHTHALMOSCOPIC FEATURES OF DIABETIC RETINOPATHY INCLUDES

Microaneurysms are seen in the macular area, the earliest detectable lesion and elsewhere in relation to area of capillary non perfusion. These are formed due to focal dilation of capillary wall following loss of pericytes.

Retinal haemorrhages both deep (dot and blot haemorrhages) and superficial haemorrhages (flame shaped) occur from capillary leakage.

Oedema characterized by retinal thickening is caused by capillary leakage.

Hard exudates yellowish white, waxy looking patches are arranged in clumps or in circinate pattern, most commonly seen in the macular area. Composed of lipoprotein and lipid filled macrophages.

Cotton wool spots are small whitish fluffy superficial lesions, represent areas of nerve fibre infarcts. If cotton wool spots more than 8 there is high risk of developing PDR.

Venous abnormalities include beading, looping and dilatation, Intraretinal microvascular abnormalities (IRMA), seen as fine irregular red lines connecting arterioles with venules, represent arteriolar-venular shunts.

Dark – blot haemorrhages representing haemorrhagic retinal infarcts.

Neovascularisation characterized by proliferation of new vessels from the capillaries as NVD or NVE

Fibrovascular formation due condensation of connective tissue around the new vessels.

Vitreous haemorrhage and vitreous detachment at later stages

Diabetic retinopathy classified as follows:-

1. Non proliferative diabetic retinopathy (NPDR)
2. Proliferative diabetic retinopathy (PDR)
3. Diabetic maculopathy
4. Advanced diabetic eye disease.

ABBREVIATED ETDRS CLASSIFICATION OF DIABETIC RETINOPATHY

Stage of diabetic retinopathy	Description
Non proliferative diabetic retinopathy (NPDR)	
Very mild	Microaneurysms only
Mild NPDR	Any or all of microaneurysm or intraretinal haemorrhage Hard/soft exudates may or maynot be present. No IRMA or venous beading
Moderate NPDR	Severe retinal haemorrhages in 1-3 quadrants or mild IRMA Significant venous beading in no more than 1 quadrant Cotton wool spots commonly present
Severe NPDR	4-2-1 rule; one or more of severe haemorrhages in all 4 quadrants Significant venous beading in 2 or more quadrants Moderate IRMA in 1 or more quadrants
Very severe NPDR	Two or more of the criteria of the severe
Proliferative diabetic retinopathy (PDR)	
Mild-Moderate PDR	New vessels on the disc(NVD) or new vessels else where (NVE), but extent insignificant to meet the high-risk criteria.
High-Risk PDR	New vessels on the disc (NVD) (about 1/3 disc area) Any NVD with vitreous or preretinal haemorrhage NVE greater than ½ disc area with vitreous or preretinal haemorrhage
Advanced diabetic Eye disease	Preretinal haemorrhage, intragel haemorrhage, tractional RD, tractional retinoschisis,rubeosis iridis

DIABETIC MACULOPATHY

Diabetic maculopathy (foveal oedema, exudates or ischemia) is the most common cause of visual impairment in diabetic patients, particularly type 2. The pathologic changes in diabetic maculopathy divided on an anatomic basis into two broad categories:-

1. Intraretinal
2. Preretinal and vitreo retinal

Intra retinal changes include macular oedema which results from increased vascular permeability and macular ischemia caused by retinal vascular occlusion.

Preretinal and vitreo retinal changes include thickening of the posterior vitreous surface and resultant new pre retinal membrane formation which from the proliferation of fibrous, glial and fibrovascular tissues and tractional detachment of the macula.

CLINICALLY SIGNIFICANT MACULAR EDEMA (CSME)

Diagnostic criteria includes

- Thickening of the retina at or within 500 micron mt of the centre of the fovea
- Hard exudates at or within 500 micron mt of the centre of the fovea
- Zone of retinal thickening of 1 disc diameter, part of which is within one disc diameter of the foveal centre.

CLINICO ANGIOGRAPHIC CLASSIFICATION OF DIABETIC MACULAR OEDEMA

- **Focal exudative maculopathy**

Characterized by microaneurysms, haemorrhages, hard exudates usually arranged in a circinate pattern. FFA reveals focal leakage with adequate macular perfusion.

- **Diffuse exudative maculopathy**

Characterized by diffuse retinal oedema and thickening throughout the posterior pole. FFA reveals diffuse leakage at the posterior pole.

- **Ischemic maculopathy**

It occurs due to microvascular occlusion. The presence of ischemia may be inferred if ophthalmoscopy shows cotton wool spots in the macula or white thread like arterioles supplying the macula but FFA is the most accurate method of evaluating the blood supply.

- **Mixed maculopathy**

Combined features of ischemic and exudative maculopathy are present.

DIABETIC MACULAR ISCHEMIA

The key symptom of ischemic maculopathy is blurred vision. Usually there are no visual symptoms until extensive capillary damage occurs in the macula. The only way of diagnosing ischemic maculopathy is by fundus fluorescein angiography.

Severity of macular ischemia graded according to the following features

1.Focal capillary drop out

2.Enlargement of foveal avascular zone

3.occlusion of arterioles.

Mild macular ischemia

1. Focal capillary drop out
2. Ophthalmoscopically: macula may appear normal
3. FFA shows: small areas of capillary non perfusion surrounded by dilated capillaries
4. Degree of capillary occlusion consistent with normal visual acuity.

Moderate macular ischemia

1. Ophthalmoscopically: macula may appear normal
2. FFA shows: enlargement of foveal avascular zone and irregularity of its margins

3. Visual acuity remains unaffected by as much as five fold increase in the area of the zone.

Severe macular ischemia

1. Ophthalmoscopically: Acute stage, retinal oedema and cotton wool spot may be seen but in late stages small white, thread like arteriole twigs may be only evidence of ischemia.
2. FFA demonstrates the extent of non perfusion
3. Visual acuity grossly affected in this stage and patient gives h/o sudden visual loss and central scotoma.

The diagnosis of macular ischemia is of prognostic importance because the visual loss with ischemia is irreversible.

FUNDUS FLUORESCEIN ANGIOGRAPHY

Chao and flocks provided the earliest description of fluorescein angiography in 1958 and it was introduced into clinical use in 1961 by Novotny & Alvis.

Principles

Fluorescene is the property of certain molecule stimulated by a light of a shorter wave length will be excited to a higher energy level and emit light of a longer wave length.

Fluorescein (sodium fluorescein) is an orange water soluble dye, hydrocarbon, when injected intravenously readily diffuses through most of the body fluids and choriocapillaries, doesnot diffuse through retinal vascular endothelium and retinal pigment epithelium, eliminated by liver and kidneys. It is excreted in the urine over 24-48 hours.

Fluorescein binding

70-85% of fluorescein molecules bind to plasma albumin. The dye molecule also binds to blood cells, predominantly deposited on the surface of the erythrocytes.

Outer Blood-retinal barrier

Fluorescein doesnot appear to penetrate to the major choroidal vessels. The choriocapillaries, however contains multiple fenestrations and pores through which flurorescein passes into the extra vascular space. Fluorescein moves readily through Bruch's membrane but on reaching the retinal pigment epithelium are blocked by intercellular tight junctions or zonula occludentes.

Inner Blood-retinal barrier

The tight junctions between retinal capillary endothelial cells, across which neither bound nor free fluorescein can pass. The inner blood-retinal barrier disruption results in leakage of both bound and free fluorescein into the extravascular space.

Filters

1. Cobalt blue excitation filter through which passes white light from the camera. The emerging blue light enters the eye end excites the fluorescein molecules in the retinal and choroidal circulation which then emit light of a longer wave length (yellow-green).
2. Yellow green barrier filter allows only the emitted yellow green fluorescent light to pass through and it blocks the blue light if reflected from the eye.

Digital angiography

Image capture in modern devices via charge coupled device (CCD) of a digital camera, with older cameras using fast black and white film, provides instant picture availability, easy storage and access.

TECHNIQUE OF FFA

Preliminaries

A good quality angiogram needs adequate pupillary dilation and clear media. The patient is asked about contraindications to FA.

Absolute contraindication

Fluorescein allergy

H/O severe reaction to any allergen is a strong relative contraindication.

Relative contraindications

Renal failure (lower the pregnancy fluorescein dose).

Allergy to iodine and seafood allergies are not contraindications to FA as fluorescein contains no iodine.

Adverse effects in FA

1. Discolouration of skin and urine.(invariable)
2. Extravasation of injected dye.
3. Itching, rash.
4. Sneezing, wheezing.
5. Vasovagal episode or syncope (usually due to anxiety)
6. Anaphylactic and anaphylactoid reactions.
7. Myocardial infraction (extremely rare)
8. Death (1:220 000).

TECHNIQUE

- The patient is seated comfortably in front of the fundus camera and sharp focusing of the fundus done to obtain a well resolved photograph, by turning the focusing dial on the camera, keeping the eye piece cross hairs in sharp focus.
- A standard venous canula should be used rather than a less secure butterfly winged infusion set. The line to be checked by flushing with normal saline to check patency and to exclude extravasation.
- Sodium fluorescein usually 3ml of 25% solution is drawn into syringe.
- Fundus colour photographs are taken.
- Red free image is captured.

- If indicated, a pre-injection study is performed to detect autofluorescence, with both the excitation and barrier filters in place.
- Images are taken at approximately 1 second intervals, beginning 5-10 seconds after injection and continuing through the desired phases.
- If the pathology is monocular, control pictures of the opposite eye should still be taken, usually after the transit phase has been photographed in one eye.
- If appropriate, late photographs may be taken after 10 minutes to show leakage, and occasionally after 20 minutes.
- Stereo images may be helpful to demonstrate elevation, and are usually taken by manually repositioning the camera sideways or by using a special device to adjust the image, such images are actually pseudostereo, true stereo requiring simultaneous pictures from differing angles.

PHASES OF ANGIOGRAM

Arm to retinal circulation time is the mean interval between injection and appearance at the optic disc. Average time is 8.5 to 11 seconds.

Angiogram consists of the following overlapping phases

1. Choroidal phases (pre arterial)
2. Arterial phase
3. Arteriovenous phase (capillary)
4. venous phase
5. Late (re circulation) phase.

Choroidal phase

Typically occurs 9-15 secs after dye injection, characterized by patchy lobular filling due to leakage of free fluorescein from the fenestrated choriocapillaries. A cilioretinal artery if present will fill at this time because is derived from posterior ciliary circulation.

Arterial phase

Starts about a second after the onset of choroidal fluorescence. Initially, only the axial segment of arterial blood fluoresces, blood plasma adjacent to the wall stains later.

Arterio-venous phase

Follows arterial filling, there is complete filling of the arteries and capillaries with early laminar flow in the veins.

Several variation of capillaries exist.

1. Radial peripapillary:- capillaries which branch perpendicularly.
2. Perifoveal capillaries:- originate from intraretinal arterioles.

These capillaries form a fine lay network capillaries at the borders of the avascular area, form a scalloped edge.

Venous phase

Retinal circulation time is the duration of time between the first detection of dye in the arterial system until the detection of dye in the tributary venous system, about 1.2 to 2.4 seconds. Venous filling is seen earliest in peripapillary and macular regions. Lamellar flow in the venous system is the reciprocal of flow in the arterial system.

Recirculation (late) phase

Demonstrates the effects of continuous recirculation, dilution and elimination of the dye. Approximately 30 seconds after injection, 1st high concentration flush of fluorescein begins to empty from choroidal and retinal circulation. Fluorescein is absent from retinal vasculature after about 10 minutes.

Staining of bruch's membrane choroid and sclera visible if RPE is lightly pigmented. Lamina cribrosa within the disc remains hyperfluorescent because of staining. Edge of the disc stains from the adjacent choriocapillaries.

INTERPRETATION OF ANGIOGRAM

The study of the FFA starts at the vitreous.

In normal angio vitreous is clear and non fluorescent. Fluorescein leaks into the vitreous when there is intraocular inflammation or retinal neovascularisation.

For FFA it is to divide the sensory retina into two layers inner vascular half and outer avascular half. Important FFA concept is that the normal retinal blood vessels does not leak fluorescein.

In FFA, RPE interpretation is important because it prevents fluorescein leakage from the choroid and also blocks choroidal fluorescence. Bruch's membrane separates RPE from the choriocapillaries, which is permeable to fluorescein. Beneath the choriocapillaries are the larger choroidal vessels, which are impermeable to fluorescein.

Two specialized areas of the fundus needs discussion:-

1. Macula
2. Optic nerve head

Macula

Contains only four layers ILM, outer plexiform layer, outer nuclear layer, layer of rods and cones. Outer plexiform layer in the macula is oblique, important factor in understanding the stellate appearance of cystoid oedema in the macula as opposed to honey comb appearance outside.

The dark appearance of the fovea is due to

1. Absence of blood vessels in FAZ
2. Blockage of background choroidal fluorescence due to high density of xanthophyll at the fovea.
3. Pigmented epithelial cells in the macula more columnar and have greater concentration of melanin and lipofuscin.

Optic nerve head

Optic disc is fed by two systems:-

1. Retinal vascular system
2. Posterior ciliary vascular system

Central retinal artery

Arises from the ophthalmic artery and it supplies the axial portion of the anterior portion of the optic nerve, short centrifugal branches from the axial portion of the CRA supplies the retrolaminar part of the optic nerve. No further branches of CRA until it reaches the retina.

Short posterior ciliary arteries

Supplies the retrolaminar portion of the optic nerve. Also lamina cribrosa is supplied by centripetal branches of SPCA.

Because most of the disc is supplied by ciliary system, fluorescein appears simultaneously at the optic nerve head and choroid, before it is apparent in the retinal arteries.

Venous drainage

Main – central retinal vein

Prelaminar – empties into both CRV and peripapillary choroid thus providing collateral drainage into CRV behind the lamina cribrosa, hence large dilated collaterals are frequently seen following CRVO and are called retinociliary veins.

ABNORMAL FFA

First step to recognize areas of abnormal fluorescence:-

1. Hypofluorescence: reduction or absence of normal fluorescence
2. Hyperfluorescence: abnormally excess fluorescence

Hypofluorescence

Any abnormally dark area of the angiographic film.

Two possible causes are

1. Blocked fluorescence (fluorescein is present but cannot be seen).
2. Vascular filling defect (Fluorescein cannot be seen because it is not present)

HYPERFLUORESCENCE

Abnormally light area on the angio or an area showing fluorescence excess.

Causes for hyperfluorescence

1. Preinjection fluorescence
2. Transmitted fluorescence
3. pooling
4. Leakage
5. Abnormal vessels

FFA CHANGES IN DIABETIC RETINOPATHY

1. Location and extent of the microaneurysms can be made out.
2. Location of hard/soft exudates seen as blocked fluorescence.
3. The areas of capillary non perfusion.
4. The extent of clinically significant macular oedema(CSME).
5. FAZ abnormalities like increased FAZ, irregularities can be made out to detect diabetic macular ischemia, difficult to diagnose clinically.
6. Presence of IRMA and its confirmation (does not leak fluorescein).
7. Presence of NVD/NVE seen as leakage.
8. Presence of collaterals can be made out (does not leak fluorescein).
9. Venoous abnormalities like beading, kinking, looping can be made out.
10. Large retinal haemorrhages produces blocked fluorescence.

ROLE OF FFA IN DIABETIC RETINOPATHY

1. To stage the retinopathy
2. To determine the extent of the lesion
3. To confirm the clinical findings
4. To detect the lesions not made out ophthalmoscopically/slit lamp biomicroscopy such as capillary dropouts / FAZ abnormalities
5. To decide about the treatment plan
6. To monitor the treatment
7. For documentation

AIM OF THE STUDY

To determine the association of risk factors like hypertension, Ischemic Heart Disease, Hyperlipidaemia, Nephropathy in Type-2 diabetic patients with Diabetic Macular Ischemia

MATERIALS AND METHODS

A cross sectional study was performed on 100 diabetic patients, attending the outpatient department of ophthalmology, Government Stanley Medical College, Chennai, during a period of one year from November 2012 to October 2013.

This study was done in accordance with the rules of ethical committee. All the subjects were explained about the nature of the procedure and a written informed consent was obtained.

INCLUSION CRITERIA

1. Type – 2 DM patients of more than 5 years duration with diabetic retinopathy/maculopathy
2. Patients with age group of more than 40 years

EXCLUSION CRITERIA

1. Type – 1 Diabetes mellitus
2. FFA not possible due to medical reasons or refusal
3. Hazy ocular media precluding good view of the Retina
4. Any prior photo coagulation in the macular region
5. Concomitant ocular pathology that could potentially influence the progression of retinopathy (Glaucoma, high Myopia, Retinitis pigmentosa and other causes of Optic Atrophy)
6. Concomitant fundus pathology that could potentially affect FAZ (Eg : Arterial / Venous Occlusion)

METHODOLOGY

Following data were collected

1. Personal data including name, age, gender
2. History of Diabetes mellitus, age of onset, duration, treatment details.
3. Medical history of hypertension / ischemic heart disease/ hyperlipidaemia or any other systemic illness.
4. Detailed ophthalmic history
5. Visual acuity by Snellen's Chart
6. Refraction
7. Slit Lamp examination of anterior segment
8. IOP by Goldman Applanation Tonometer
9. Dilated Fundus evaluation with direct ophthalmoscope, slit lamp biomicroscopy with 90D, indirect Ophthalmascopy
10. Diabetic retinopathy graded based on an abbreviated ETDRS severity scale (Mild, Moderate severe & very Severe) non-proliferative diabetic retinopathy (NPDR); early and high PDR
11. Fundus Fluorescein Angiography was done using 3 ml of 20% Sodium Fluorescein dye, following the due procedure
12. Foveal avascular zone assessed from the frames during the capillary phase

13. Physician Opinion obtained to rule out hypertension, renal disease, ischemic heart disease and hyper lipidemia
14. The laboratory tests included:
    - Fasting and post prandial plasma glucose levels,
    - Glycosylated haemoglobin (HbA1c) levels
    - Fasting plasma lipid profile
    - The blood urea and serum creatinine levels
    - Routine urine examination to r/o albuminuria
    - Electrocardiogram (ECG)
    - Echocardiogram, if needed as suggested by the cardiologist.

Glycemic status of the patient was assessed by

1. Fasting plasma glucose level
2. Post prandial plasma glucose level with antidiabetic agents
3. HbA1C done to assess the glycemic control

HbA1c shows the average blood sugar level over the past three months. HbA_1 refers to the non-enzymatic binding of several species of carbohydrate to haemoglobin, whereas in HbA_{1c} the carbohydrate is specifically glucose[28]. When HbA1c levels are more than 6.5%, taken as uncontrolled glycemic status as per American diabetes association (ADA) 2013 guidelines[29].

Blood pressure was recorded by sphygmomanometer in the upper arm, in sitting posture after 10 minutes of rest.

The JNC criteria 7[30] followed to define systemic hypertension:

1. Either a systolic BP of ≥140 mm Hg
2. Or diastolic BP of ≥90 mm Hg
3. Or the patient already on anti-hypertensive medications.

Criteria for nephropathy was

1. Presence of urine albuminuria and/or
2. Blood urea >40mg/dl and/or
3. Serum creatinine >1.5mg/dl.

Criteria for hyperlipidaemia was

1. Fasting plasma cholesterol level of more than 200mgs/dl

Ischemic heart disease (IHD) was diagnosed,based on ECG changes as

1. Elevation/depression of ST segment,
2. Inversion of 'T' wave supported by echographic findings and
3. History of previous attacks or cardiovascular surgery or angioplasty for IHD.

Fundus fluorescein angiography

Study subjects were assessed for the presence of macular Ischemia confirmed by fundus fluorescein Angiography.We followed the criteria described by Bresnick et al[4] based on fundus fluorescein angiography to define macular ischemia.

1. **Mild irregularities** considered as small breaks in the margin of FAZ seen as deep undulations.
2. **Moderate irregularities** defined as abnormally dilated and tortuous capillaries budding into the FAZ, terminal arterioles/venules directly abutted FAZ margins and enlarged inter capillary spaces around FAZ.
3. **Severe irregularities** were defined as FAZ architecture grossly enlarged FAZ with pruned off arterioles.

Normal FAZ: defined as FAZ <1000 micron in the longest diameter, regular and round/horizontally oval in shape.

Datas collected were entered and stored in the Microsoft excel sheet 2007.

DATA ANALYSIS

Descriptive analysis of all the explanatory variables including Age, Sex, diabetes control and other systemic diseases was done. All the explanatory variables with statistically significant association in univariate analysis were included in the multivariate regression analysis to calculate adjusted odds ratios for the individual factors. The 95% CI and P- value for the same were computed by using multivariate logistic regression analysis. P- value less than 0.05 was taken as the cut off level to determine statistical significance.

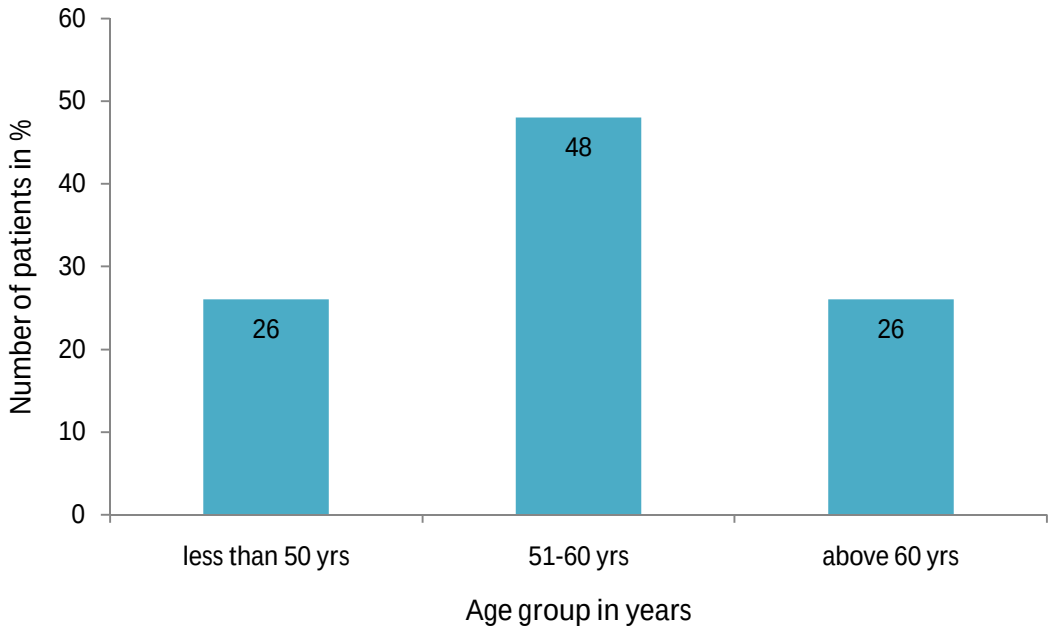
OBSERVATION AND RESULTS

A total of 100 patients, all of them who were suffering from type 2 diabetes mellitus of more than 5 years duration with diabetic retinopathy were included in the final analysis. Each eye of the individuals was taken as a unit for further statistical analysis i.e a total of 200 eyes was included in the analysis. Out of total 200 eyes examined 52(26%) belonged to 50 years or below age group. The proportion of examined eyes between 51 to 60 years and above 60 years were 48% and 26% respectively. Females constituted 110 (55%) and males constituted 90 (45%) of the sample. (Table 1)

Parameter	Frequency	Percent
I. Age group		
<= 50 yrs	52	26.0
51 to 60 yrs	96	48.0
Above 60 years	52	26.0
Total	200	100.0
II.Gender		
Female	110	55.0
Male	90	45.0
Total	200	100.0

FIGURE 1

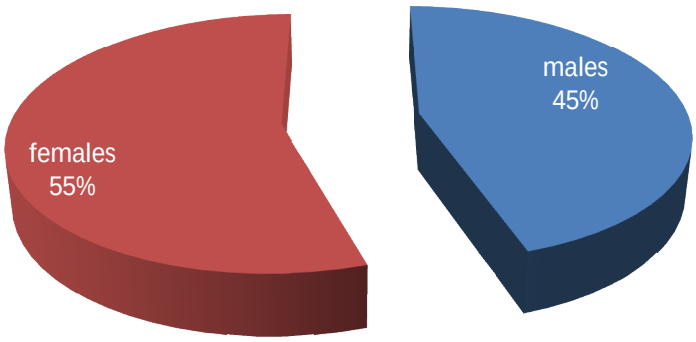
AGE DISTRIBUTION



Out of 100 subjects, 26 subjects (26%) belonged to less than 50 years age group, 48 subjects (48%) belonged to 51-60 years age group and (26%) belonged to above 60 years age group.

FIGURE 2

SEX DISTRIBUTION

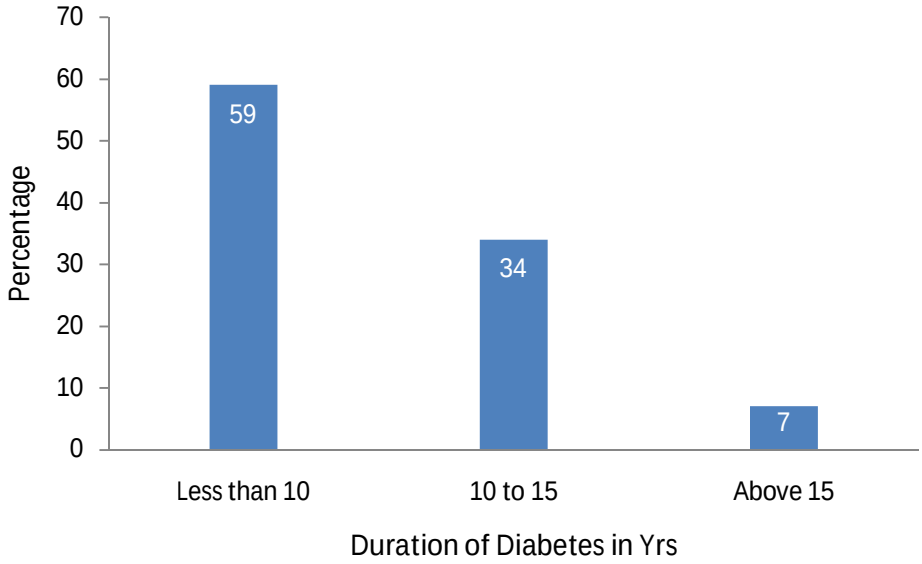


Females constituted – 55%

Males constituted – 45%

FIGURE 3

DURATION OF DIABETES MELLITUS (N= 100)



Out of the 200 eyes examined, the duration of Diabetes mellitus was less than 10 years in 59% of the patients, 10 to 15 years in 34% and more than 15 years in 7%. (Figure 3)

TABLE 2

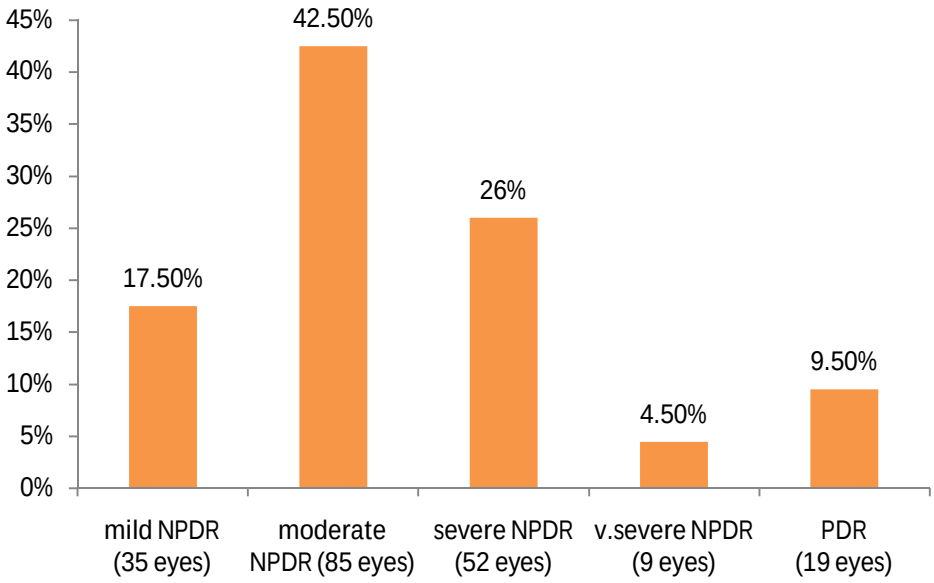
PREVALENCE OF OTHER SYSTEMIC DISEASES IN THE STUDY GROUP (N= 200)

Parameter	Frequency	Percent
I. Hypertension		
Present	130	65.0
Absent	70	35.0
II. Hyperlipidaemia		
High	118	59.0
Normal	82	41.0
III. Ischemic heart disease		
Present	42	21.0
Absent	158	79.0
IV. Nephropathy		
Present	78	39.0
Absent	122	61.0

The prevalence of other systemic diseases was analyzed. Hypertension was present in 65% of the study subjects. Hyperlipidaemia, ischemic heart disease and nephropathy were present in 59%, 21% and 39% of study participants respectively. (Table 3)

FIGURE 4

PRESENTATION OF VARIOUS STAGES OF DIABETIC RETINOPATHY IN % (N= 200)



Out of 200 eyes examined about 35 eyes(17.5%) had mild NPDR changes, 85 (42.50%) eyes had moderate NPDR changes, 52 eyes(26%) showed severe NPDR changes, 9 eyes (4.5%) had very severe NPDR changes and 19eyes (9.5%) had PDR changes.

TABLE 3

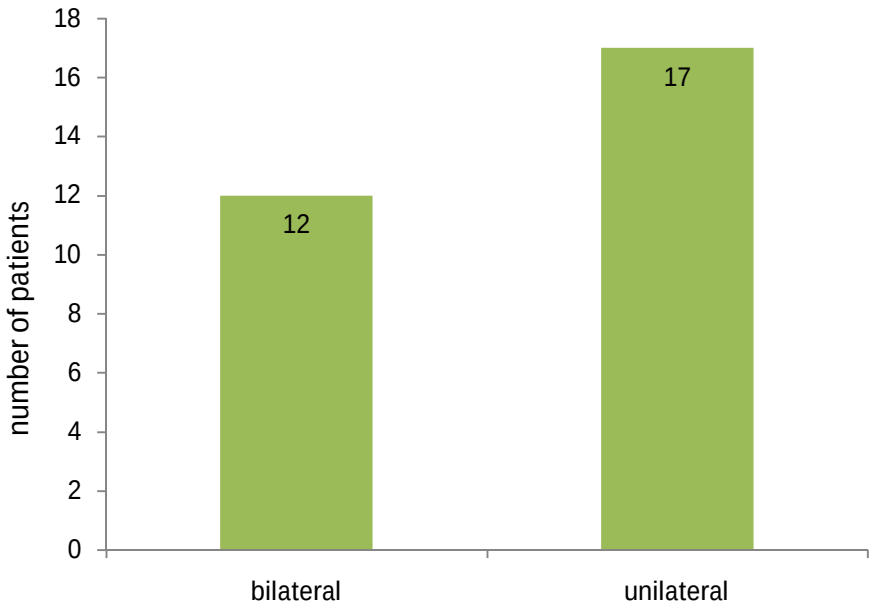
PREVALENCE OF DIABETIC MACULAR ISCHEMIA IN THE STUDY GROUP (N= 200)

Macular Ischemia	Frequency	Percent
Present	41	20.5
Absent	159	79.5
Total	200	100.0

The prevalence of diabetic macular ischemia as defined by fundus fluorescein angiography findings was 20.5% in the study population. (Table 2).

FIGURE 5

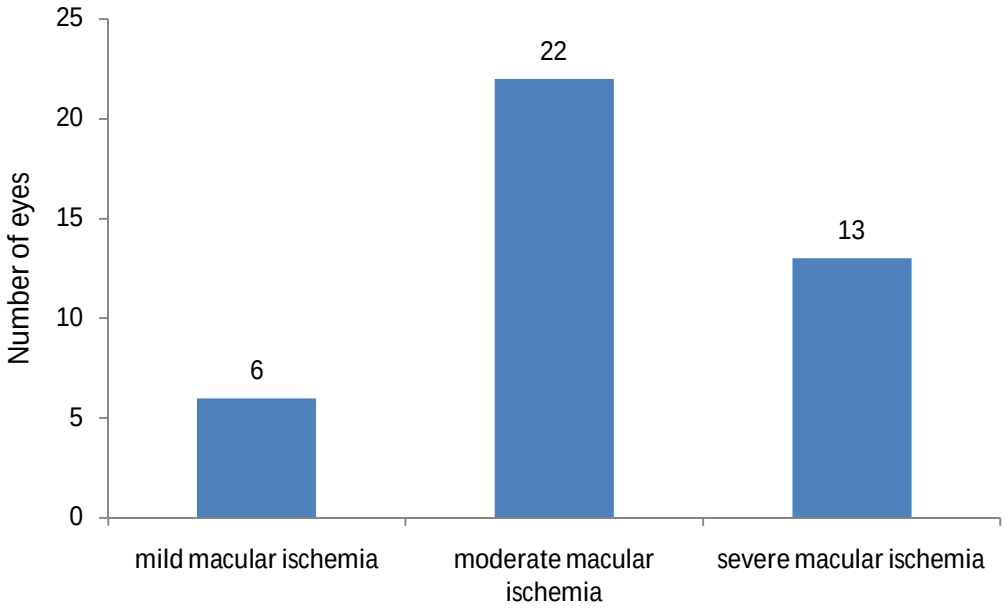
LATERALITY



Out of 41 eyes 12 patients (24 eyes) had bilateral diabetic macular ischemia and 17 patients (17 eyes) had unilateral diabetic macular ischemia.

FIGURE 6

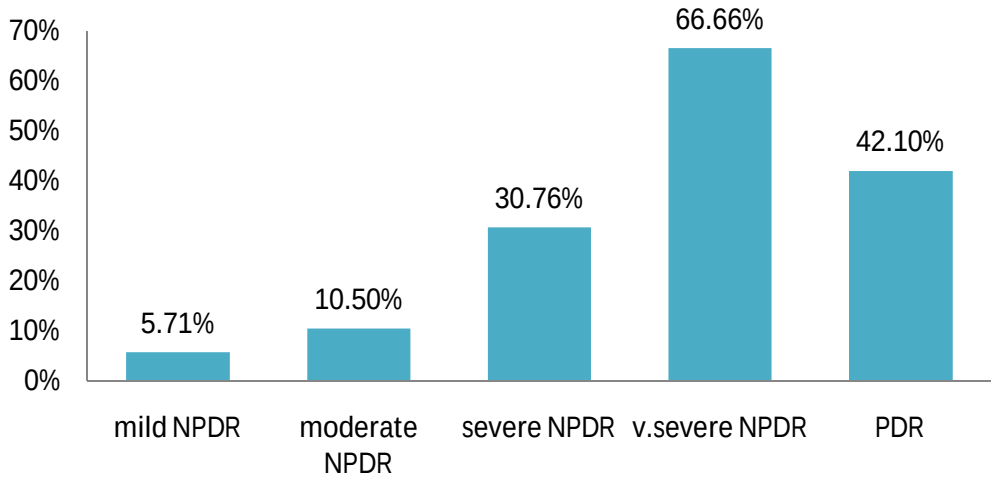
PREVALENCE OF DIFFERENT GRADES OF DIABETIC MACULAR ISCHEMIA



Out of 41 eyes with diabetic macular ischemia, mild irregularities noted in 6 eyes, moderate irregularities noted in 22 eyes and increased FAZ noted in 13 eyes.

FIGURE 7

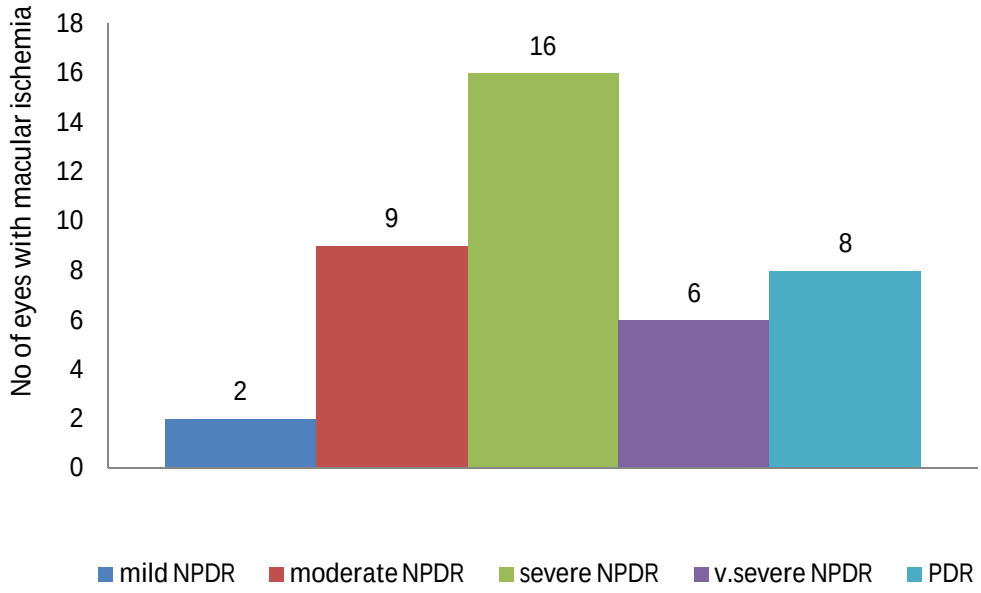
PREVALENCE OF DIABETIC MACULAR ISCHEMIA WITHIN DIFERRENT STAGES OF DIABETIC RETINOPATHY



Out of 200 eyes within different grades of retinopathy, the prevalence of diabetic macular ischemia noted in mild NPDR stage was 5.71%(n=35), moderate NPDR stage was 10.50%(n=85), severe NPDR was 30.76%(n=52), very severe NPDR stage was 66.66%(n=9) and in PDR stage was 42.10%(n=19).

FIGURE 8

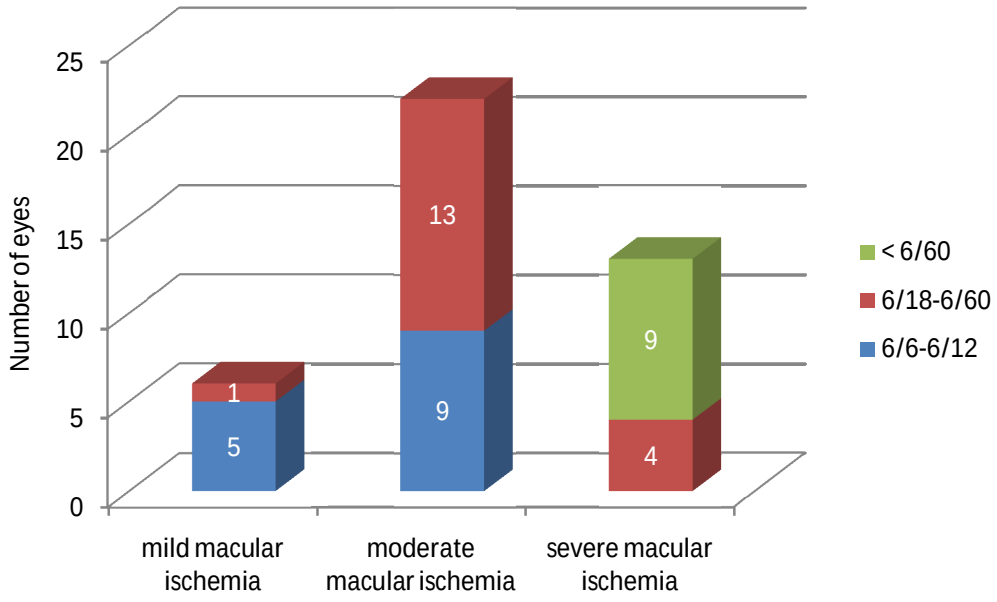
PREVALENCE OF DIABETIC MACULAR ISCHEMIA IN VARIOUS STAGES OF DIABETIC RETINOPATHY



Out of 41 eyes examined, it was observed that 2 eyes(4.8%) in mild NPDR stage, 9 eyes (2I.95%) in moderate NPDR stage, 16 eyes(39.02%) in severe NPDR stage, 6 eyes (14.63%) in very severe NPDR stage and 8 eyes, (19.51%) in PDR stage showed macular ischemia.

FIGURE 9

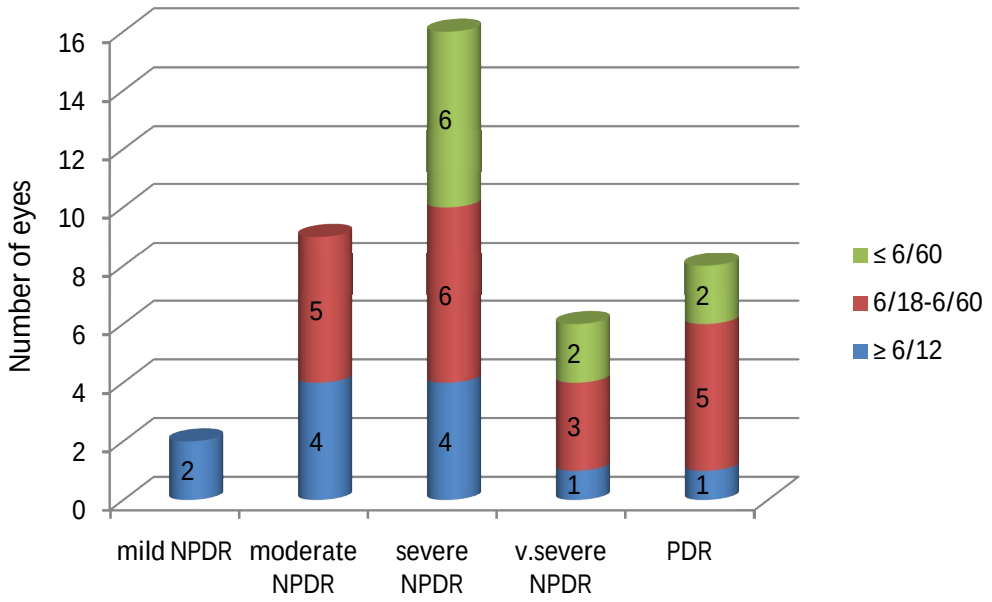
VISUAL ACUITY PRESENTATION IN DIFFERENT GRADES OF DIA MACULAR ISCHEMIA



- Out of 6 eyes with mild macular ischemia, 5 had V/A of > 6/12 (83.3%) and 1 had V/A of 6/18-6/60 (16.7%).
- Out of 22 eyes with moderate macular ischemia, 9 had V/A of > 6/12 (40.90%) and 13 had V/A of 6/18-6/60 (59.1%) and
- Out of 13 eyes with severe macular ischemia, 4 had V/A of 6/18-6/60 (30.76%) and 9 had V/A of < 6/60 (69.23%).

FIGURE 10

PRESENTATION OF VISUAL ACUITY IN DIFFERENT STAGES OF DIABETIC RETINOPATHY



Analysis of visual acuity of the subjects with macular ischemia(n=41), we noted that

- In mild NPDR stage out of 2 eyes, both of them had V/A of ≥ 6/12,
- In moderate NPDR out of 9 eyes, 4 had V/A of ≥ 6/12(44.45%) and 5 had V/A of 6/18-6/60(55.55%),
- In severe NPDR stage out of 16 eyes 4 had V/A of ≥ 6/12(25%), 6 had V/A of 6/18-6/60(37.5%) and 6 had V/A of ≤ 6/60(37.5%),

- In v.severe NPDR stage out of 6 eyes 1 had V/A of ≥ 6/12(16.67%), 3 had V/A of 6/18-6/60(50%) and 2 had V/A of ≤ 6/60(33.33%) and
- In PDR stage out of 8 eyes 1 had V/A ≥ 6/12(12.50%), 5 had V/A of 6/18-6/60(62.5%) and 2 had V/A of ≤ 6/60(25%).

TABLE 4

ASSOCIATION BETWEEN AGE GROUP AND SEX VARIABLES WITH DIABETIC MACULAR ISCHEMIA

Parameter		**Macular Ischemia**		**Unadjusted OR**	**95% CI**		**p-value**
		Present	**Absent**		**Lower**	**Higher**	
Age group	<=50	11(21.2%)	41(78.8%)	1			
	51 to	19(19.8%)	77 (80.2%)	.920	.400	2.117	.920
	>= 61	11(21.2%)	41(78.8%)	1.000	.390	2.563	1.000
Sex	Male	73	17(18.9%)	1			
	Female	86(78.2%)	24(21.8%)	1.198	.598	2.402	.610

The odds of macular ischemia were almost similar in different age groups. Gender had not shown any significant difference influence on odds of macular ischemia. (Table 4)

TABLE 5

ASSOCIATION BETWEEN DURATION OF DIABETES, GLYCEMICCONTROL AND DIABETIC MACULAR ISCHEMIA

Parameter		**Macular Ischemia**		**Unadjusted OR**	**95% CI**		**p-value (Chi square test)**
		Present	Absent		**Lower**	**Higher**	
Duration of diabetes mellitus	More than 15 years	5 35.7%	9 64.3%	1			
	Less than 15 years	36 19.4%	150 80.6%	.432	.136	1.367	.15
HBa1c (gm%)	>6.5	32 33.3%	64 66.7%	**5.3**	2.4	11.8	**.00**
	Less than 6.5	9 8.7%	95 91.3%	1			

Duration of diabetes mellitus had no significant impact on the occurrence of macular ischemia. But the odds of macular ischemia were 5.3 times higher in patients with poorly controlled diabetes mellitus with Hba1c level more than 6.5gm% (OR 5.3, 95% CI 2.4 to 11.8, p value < 0.01)

TABLE 6

ASSOCIATION BETWEEN VARIOUS OTHER SYSTEMIC DISEASES AND DIABETIC MACULAR ISCHEMIA

Systemic Disease		Macular Ischemia		Unadjusted OR	95% CI		p-value (Chi square test)
		Present	Absent		Lower	Higher	
HTN	Present	29 22.3%	101 77.7%	1.388	.658	2.927	.389
	Absent	12 17.1%	58 82.9%	1			
Hyperlipidaemia	High	21 17.8%	97 82.2%	1.490	.747	2.972	.258
	Normal	20 24.4%	62 75.6%	1			
Ischemic heart Disease (IHD)	Present	6 14.3%	36 85.7%	1.7	0.7	4.4	0.3
	Absent	35 22.2%	123 77.8%	1			
Nephropathy	Present	30 38.5%	48 61.5%	**6.3**	2.92	13.6	**.00**
	Absent	11 9.0%	111 91.0%	1			

The association between presence of other systemic diseases and occurrence of macular ischemia was assessed. Presence of nephropathy had increased the odds of macular ischemia 6.3 times when compared to people without nephropathy (OR 6.3, 95% CI2.9 to 13.6, p value < 0.01). The Presence of other systemic diseases had no significant influence on odds of macular ischemia. (Table 6).

TABLE 7

MULTIVARIATE LOGISTIC REGRESSION ANALYSIS OF ASSOCIATION OF VARIOUS SCOIO DEMOGRAPHIC AND SYSTEMIC DISEASES WITH MACULAR ISCHEMIA (N= 200)

	Adjusted ODDS RATIO	P- Value	95% C.I. for Odds Ratio	
			Lower	Upper
I.Agegroup				
<= 50 yrs (Baseleine)				
51 to 60 yrs	1.055	.912	.409	2.718
Above 60 years	1.491	.487	.484	4.593
II.Gender				
Male (Baseline)				
Female	.759	.500	.340	1.693
III.Duration of diabetes mellitus				
>15 yrs(Baseline)				
<=15 yrs	1.529	.539	.394	5.930
IV.Hba1c				
Controlled(Baseline)				
Uncontrolled	**2.9**	**.022**	1.2	7.4
V.HTN				
Absent (Baseline)				
present	1.291	.554	.554	3.011
VI. Ischemic heart Disease (IHD)				
Absent (Baseline)				
present	.673	.476	.226	2.001
VII. Hyperlipidaemia				
Normal (Baseline)				
High	1.688	.201	.757	3.764
VIII. Nephropathy				
Absent (Baseline)				
Present	**4.5**	**.001**	1.8	11.0

Multivariate logistic regression analysis was done to assess the influence of various socio demographic, diabetes related parameters and various systemic diseases on occurrence of macular ischemia. After adjusting for the effect of all other variables in the equation the odds of macular ischemia were 4.5 times higher in patients with nephropathy (Adjusted OR 4.5,95 CI(1.8-11.0),P value .001) and the diabetic macular ischemia were 2.9 times higher in patients with poorly controlled diabetes mellitus with HbA1c level more than 6.5gm% (Adjusted OR 2.9, 95% CI(1.2-7.4),(p value .022) (Table 7).

DISCUSSION

- In this study out of 100 subjects 26% belonged to 50 years or below age group, 48% belonged to 51-60 years age group, 26% belonged to above 60 years age group. (Figure 1)
- Females constituted 55% and males constituted 45% of the sample.(Figure 2)
- Out of the 200 eyes examined, the duration of Diabetes mellitus was less than 10 years in 59% of the patients, 10 to 15 years in 34% of patients and more than 15 years in 7% of patients. (Figure 3)
- Hypertension was present in 65% of the study subjects. Hyperlipidaemia, coronary artery disease and nephropathy were present in 59%, 21% and 39% of study participants respectively. (Table 2)
- Out of 200 eyes examined about 35 eyes(17.5%) had mild NPDR changes, 85 (42.50%) eyes had moderate NPDR changes, 52 eyes(26%) showed severe NPDR changes, 9 eyes (4.5%) had very severe NPDR changes and 19eyes (9.5%) had PDR changes.(Figure 4)
- Out of 200 eyes examined 41 eyes showed diabetic macular ischemia accounted for 20.5% of eyes with diabetic retinopathy.(Table 3)

- Macular ischemia was bilateral in 12 patients (24 eyes) and unilateral in 17 patients (17 eyes). (Figure 5)

Out of 41 eyes with diabetic macular ischemia (Figure 6)

1. Mild irregularities noted in 6 eyes (14.63%),
2. Moderate irregularities noted in 22 cases(53.65%) and
3. Increased FAZ noted in 13 cases(31.70%).

- Out of 200 eyes within different grades of retinopathy, the prevalence of diabetic macular ischemia noted in mild NPDR stage was 5.71%(n=35), moderate NPDR stage was 10.50%(n=85), severe NPDR was 30.76%(n=52), very severe NPDR stage was 66.66%(n=9) and in PDR stage was 42.10%(n=19) (Figure 7). This showed that diabetic macular ischemia is more prevalent in severe stages of diabetic retinopathy.

- Out of 41 eyes with diabetic macular ischemia, it was observed that 2 eyes(4.8%) in mild NPDR stage (n=41), 9 eyes (2I.95%) in moderate NPDR stage(n=41), 16 eyes(39.02%) in severe NPDR stage(n=41), 6 eyes (14.63%) in very severe NPDR stage(n=41) and 8 eyes(19.51%) in PDR stage(n=41) showed macular ischemia.(Figure 8). This showed that diabetic macular ischemia is more prevalent in severe stages of diabetic retinopathy.

STUDY	OBSERVATIONS
Shukla et al	DMI was prevalent in 36% in eyes with mild-moderate NPDR,63% in eyes with early proliferative retinopathy and 70% in high-risk retinopathy
Sim et al	DMI was prevalent in mild-moderate NPDR stage was 46%, severe NPDR stage was 59.7%, and in PDR stage was 77.2%.
Our study	DMI was prevalent in mild NPDR stage was 5.71%, moderate NPDR stage was 10.50%,severe NPDR stage was 30.76%, v.severe NPDR stage was 66.66% and in PDR stage was 42.10%.

- Shukla et al study[1] also reported that diabetic macular ischemia was more common in severe stages of retinopathy, comparable to our study.
- Sim et al[5] reported that DMI was most prevalent in eyes with proliferative diabetic retinopathy.
- Our study also showed that DMI was more prevalent in severe stages of retinopathy.

Visual acuity assessment of the subjects with diabetic macular ischemia showed (Figure 9)

- Out of 6 eyes with mild macular ischemia, 5 had V/A of > 6/12 (83.3%) and 1 had V/A of 6/18-6/60 (16.7%).
- Out of 22 eyes with moderate macular ischemia, 9 had V/A of > 6/12 (40.90%) and 13 had V/A of 6/18-6/60 (59.1%) and
- Out of 13 eyes with severe macular ischemia, 4 had V/A of 6/18-6/60 (30.76%) and 9 had V/A of < 6/60 (69.23%).

STUDY	OBSERVATIONS
Sim et al	8/23 eyes (34.8%) in severe; 7/45 eyes (15.6%) in moderate; 11/103 eyes (10.7%) in mild macular ischemia showed decreased visual acuity.
Our study	9/13 eyes (69.23%) in severe DMI; 13/22 eyes (59.1%) in moderate DMI; 1/6 eyes (16.7%) in mild diabetic macular ischemia showed decreased visual acuity.

- Sim et al[5] reported that diabetic macular ischemia is associated with reduced V/A in eyes with moderate to severe ETDRS-DMI grades of ischemia but preserved in milder grades.

- Our study also showed that reduced visual acuity in moderate to severe grades of diabetic macular ischemia and good visual acuity maintained in milder grades of ischemia.

Analysis of V/A of the subjects with macular ischemia (Figure 10) within different stages of diabetic retinopathy we noted that,

- In mild NPDR stage out of 2 eyes, both of them had V/A of ≥ 6/12,
- In moderate NPDR out of 9 eyes, 4 had V/A of ≥ 6/12 (44.55%) and 5 had V/A of 6/18-6/60 (55.55%),
- In severe NPDR stage out of 16 eyes 4 had V/A of ≥ 6/12(25%), 6 had V/A of 6/18-6/60(37.5%) and 6 had V/A of < 6/60(37.5%).
- In v.severe NPDR stage out of 6 eyes 1 had V/A of ≥ 6/12(16.67%), 3 had V/A of 6/18-6/60(50%) and 2 had V/A of < 6/60(33.3%) and
- In PDR stage out of 8 eyes 1 had V/A ≥ 6/12(12.50%), 5 had V/A of 6/18-6/60(62.5%) and 2 had V/A of < 6/60 (25%).

This showed that decreased visual acuity is observed more in severe grades of diabetic retinopathy with diabetic macular ischemia.

ANALYSIS OF ASSOCIATION OF RISK FACTORS IN DIABETIC MACULAR ISCHEMIA

Age and gender

On analysis of our study the odds of macular ischemia were almost similar in different age groups. Gender had not shown any significant difference influence on odds of macular ischemia. (Table 4)

STUDY	OBSERVATION
Shukla et al	Age group: p value 0.59; Gender: p value 0.40
Our study	Age group: p value 0.92; Gender: p value 0.61

- Shukla et al study[1] reported that there were no significant differences in age and gender.
- Our study also reported that there was no significant differences in age and gender.

Duration of diabetes mellitus

Duration of diabetes mellitus either more than 15 years or less than 15 years had no significant impact on the occurence of macular ischemia. (Table 5).

STUDY	OBSERVATION
Shukla et al	P value 0.06, statistically not significant
Our study	P value 0.15, statistically not significant

- Shukla et al[1] study reported that there were no significant differences in duration of diabetes.
- Our study also showed that duration of diabetes mellitus had no significant impact on the occurence of macular ischemia.

Poor glycemic control

The odds of macular ischemia were 5.3 times higher in patients with poorly controlled diabetes mellitus with HbA1c level more than 6.5gm% (OR 5.3, 95% CI 2.4 to 11.8, p value < 0.01) (Table 5)

Shukla et al[1] reported that there was no significant association of macular ischemia and poor glycemic control.

Nephropathy

Our study analysis showed that in type 2 diabetic patients the association of macular ischemia and diabetic nephropathy was found to be statistically significant, about 4.5 times higher in patients with diabetic nephropathy.

STUDY	OBSERVATION
Shukla et al	(OR 2.62, 95%CI 1.16-5.92, P-value .011), strong correlation between macular ischemia and retinopathy
Our study	(OR 4.5, 95%CI 1.8-11.0, P-value .001), also indicates strong correlation between macular ischemia and retinopathy

- Shukla et al[(1)] reported that there was a strong positive correlation between macular ischemia and diabetic nephropathy and reported macular ischemia as a marker for nephropathy in diabetic retinopathy.
- Bresnick et al[(2)] previously found the association between retinal ischemia and nephropathy, 6 out of 8 diabetic patients with retinal and macular ischemia had elevated serum creatinine.

The association of diabetic macular ischemia and diabetic nephropathy can be explained by the similar micro angiopathic changes

occurring at the end arteries of both the retina and kidneys. Similar to changes that occurring at capillary basement membrane of the retinal arterioles, renal glomeruli also shows basement membrane thickening resulting in glomerular hyalinization resulting in ischemia.

Hypertension/IHD/Hyperlipidaemia

The association between diabetic macular ischemia and other systemic risk factors like Hypertension(OR:1.38;CI:.658-2.927),IHD(OR:1.7;CI:0.7-4.4),hyperlipidaemia (OR: 1.49; CI:.747-2.97) were not found to be as significant as diabetic nephropathy (Table 6).

STUDY	OBSERVATION
Shukla et al	Hypertension (OR: 1.05; 95% CI: 0.48 to 2.32), IHD (OR: 1.125; 95% CI: 0.45 - 2.82) and hyperlipidaemia (OR: 1.63; 95% CI: 0.72 - 3.70) were not significantly associated with macular ischaemia
Our study	Hypertension(OR:1.38;CI:.658-2.927),IHD(OR:1.7;CI:0.7-4.4), hyperlipidaemia (OR: 1.49; CI:.747-2.97) were not found to be statistically significant

- Shukla et al[1] reported that Hypertension (OR: 1.05; 95% CI: 0.48 to 2.32), IHD (OR: 1.125; 95% CI: 0.45 - 2.82) and hyperlipidaemia (OR: 1.63; 95% CI: 0.72 - 3.70) were not significantly associated with macular ischaemia, comparable to our study.

- Mansour et al[9] reported that there is no correlation of hypertension with FAZ irregularities.

MULTIVARIATE LOGISTIC REGRESSION ANALYSIS OF ASSOCIATION OF VARIOUS RISK FACTORS

Comparison between multivariate logistic regression analysis of shukla et al and our study

Variable	Shukla et al		Our study	
	OR	CI(95%) for OR	OR	CI(95%) for OR
Age	1.01	0.95-1.07	1.055	0.409-2.718
DM duration	0.96	0.90-1.03	1.529	0.394-5.930
Hypertension	0.94	0.39-2.26	1.291	0.554-3.011
IHD	1.14	0.40-3.21	0.673	0.226-2.001
Hyperlipidaemia	1.40	0.56-3.50	1.668	0.757-3.764
Nephropathy	**2.83**	1.15-7.00	**4.5**	1.80-11.00
Uncontrolled DM	-	-	**2.9**	1.20-7.40

- The association of diabetic macular ischemia with nephropathy remains most significant about 4.5 times higher after adjusting all the variables including HTN, IHD, hyperlipidaemia, duration of diabetes and uncontrolled blood sugar as shown in multivariate logistic regression analysis (OR 4.5, 95%CI 1.8-11.0, P-value .001). This is comparable to shukla study as shown in the comparison table above.

- The association of diabetic macular ischemia were 2.9 times higher in patients with poorly controlled diabetes mellitus with Hba1c level more than 6.5gm% (Adjusted OR 2.9, 95% CI(1.2-7.4),(p value .022)

This study showed that the severity of diabetic retinopathy was a major confounding variable and increased FAZ size and irregularities are known to increase with increasing severity of diabetic retinopathy.

In this study we found that the association of diabetic macular ischemia is found to be statistically significant with nephropathy and uncontrolled diabetes mellitus. All those patients found to have nephropathy referred to nephrologist for detailed evaluation of the renal status and to the diabetologist for control of blood sugar.

Also we found that visual acuity is preserved in milder grades of macular ischemia. Patients diagnosed to have diabetic macular ischemia are regularly followed up to rule out progression of the disease and to reduce the visual morbidity.

CONCLUSION

- Patients with diabetic macular ischemia also suffer from other systemic illness, the most significant associated risk factor being diabetic nephropathy, followed by uncontrolled glycemic status.

- The association between diabetic macular ischemia and other systemic risk factors like Hypertension, IHD, hyperlipidaemia were not found to be as significant as diabetic nephropathy.

- Diabetic macular ischemia was more prevalent in severe grades of retinopathy and visual acuity grossly affected in severe diabetic macular ischemia.

- Fundus Fluorescein Angiography is the diagnostic tool to assess the ischemic status of the macula irrespective of the stage of retinopathy and earlier diagnosis of diabetic macular ischemia results in preservation of visual acuity by controlling the predictive risk factors like uncontrolled diabetes mellitus and nephropathy.

- This presence of association between the poor glycemic control and diabetic macular ischemia suggests that HbA1c levels to be maintained below < 6.5% and patients with poor glycemic control referred to diabetologist for glycemic control.

- The presence of strong association between diabetic macular ischemia and nephropathy suggests that Diabetic Macular Ischemia serves as a marker of nephropathy.

- The diagnosis of diabetic macular ischemia in type 2 diabetic patients, irrespective to the stage or severity of retinopathy should alert the ophthalmologist to see the renal status of the patient to rule out nephropathy.

- Patients diagnosed to have diabetic macular ischemia are regularly followed up to rule out progression of the disease or deterioration of visual acuity.

PROFORMA

S.NO DATE :

OP.NO

NAME

AGE/SEX

ADDRESS: PHONE NO

COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

PAST HISTORY : GLASSES

SURGICAL / LASER

DIABETES : DURATION

OHA DETAILS

INSULIN

GLYCEMIC STATUS

COMORBID CONDITIONS : HTN / DYSLIPIDAEMIA / CAD / RENAL DISEASE/

PERSONAL HISTORY:

FAMILY HISTORY:

Consanguinity / glaucoma / DM / Squint / other eye affections

GENERAL PHYSICAL AND SYSTEMIC EXAMINATION :

OCULAR EXAMINATION :

FACIAL SYMMETRY :

HEAD POSTURE :

ORTHOPHORIA :

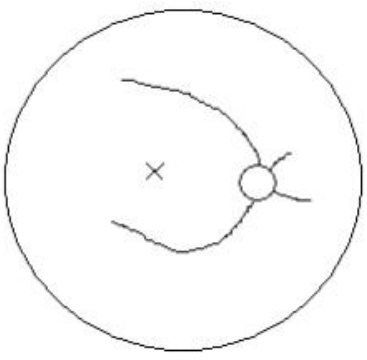
SLIT LAMP EXAMINATION:	RIGHT EYE	LEFT EYE
EYEBROWS		
EYELIDS		
CONJUNCTIVA		
CORNEA		
AC		
IRIS		
PUPIL		
LENS		
ANT.VITREOUS		
EOM		
VISUAL ACUITY (naked)		
With PH		
With glasses		
IOP		

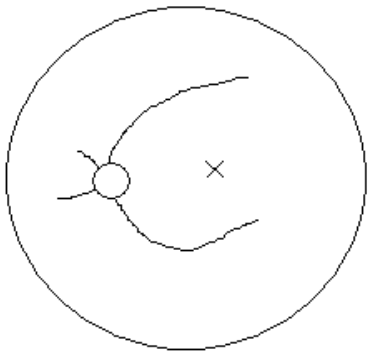
RETINOSCOPY:

SUBJECTIVE:

PMT

FUNDUS : RE LE





DIAGNOSIS :

INVESTIGATIONS :

- FBS
- PPBS
- HbA1C
- Blood urea
- Serum creatinine
- Lipid profile
- Urine sugar
- ECG
- FFA

FUNDUS FLUORESCEIN ANGIOGRAM RESULTS :

Arm to Retina Circulation time -

AV Transit Time -

FFA Finding	Right Eye	Left Eye
Choroidal Fluorescence		
Arterial Filling		
Laminar Venous Filling		
Late venous filling		
Late phase		
Foveal Avascular Zone		
Disc		
Other Findings		

ANALYSIS OF RESULTS	RIGHT EYE	LEFT EYE	RISK FACTORS PRESENT
ETDRS Grading of Retinopathy			
FFA Finding			

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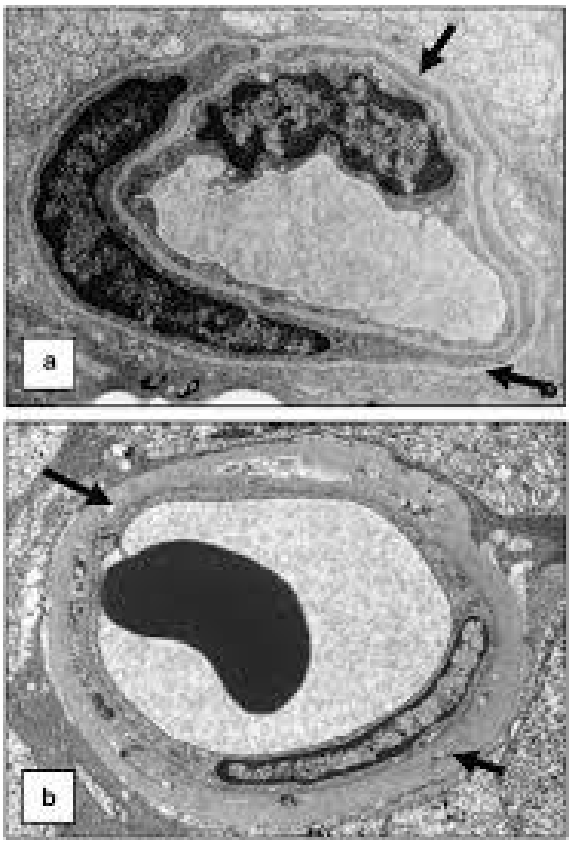


Basement Membrane Thickening Seen in Fig.b

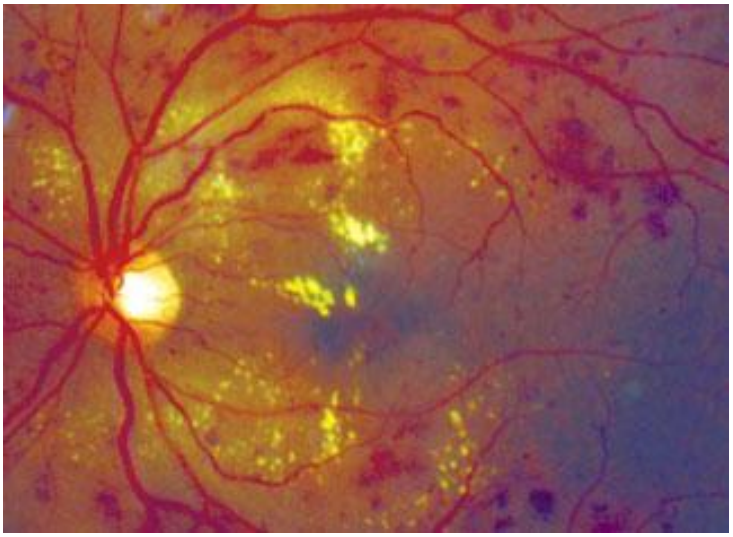
TRYPSIN DIGEST PREPARATION

Normal Endothelial Pericyte Ratio (1:1)

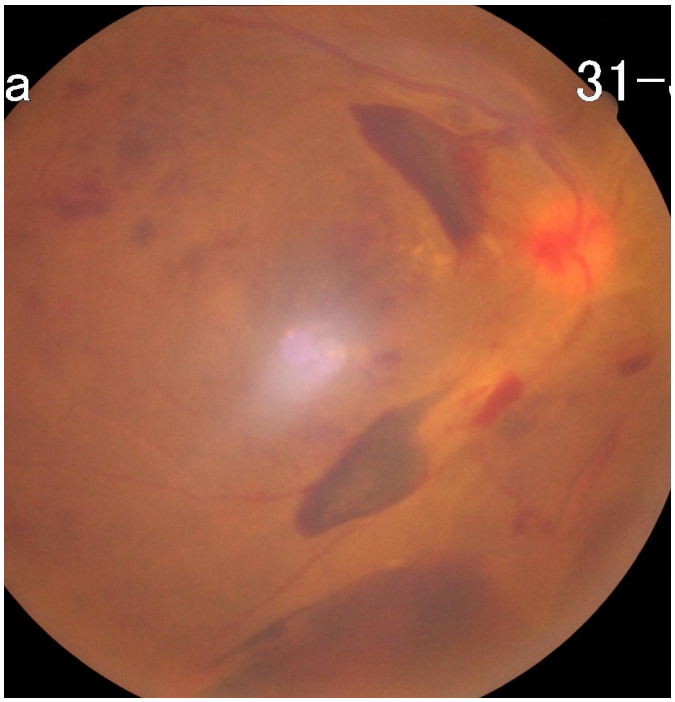
Pericyte Loss in Diabetes

Mild NPDR

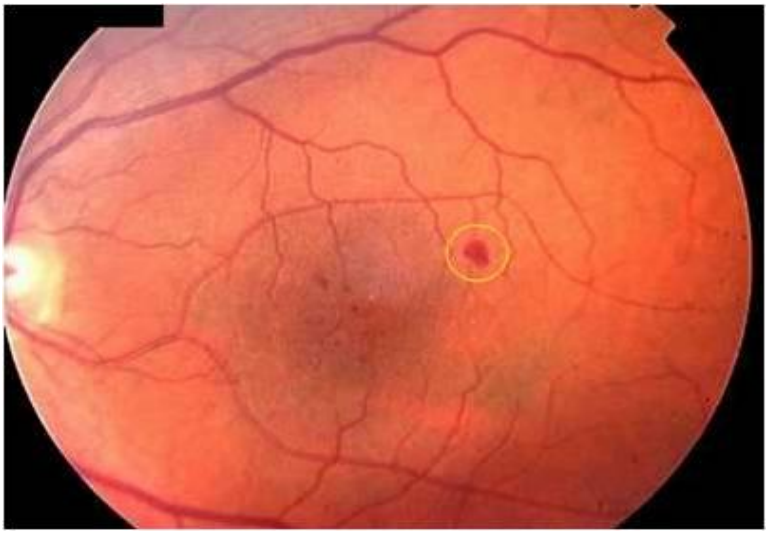
Moderate NPDR



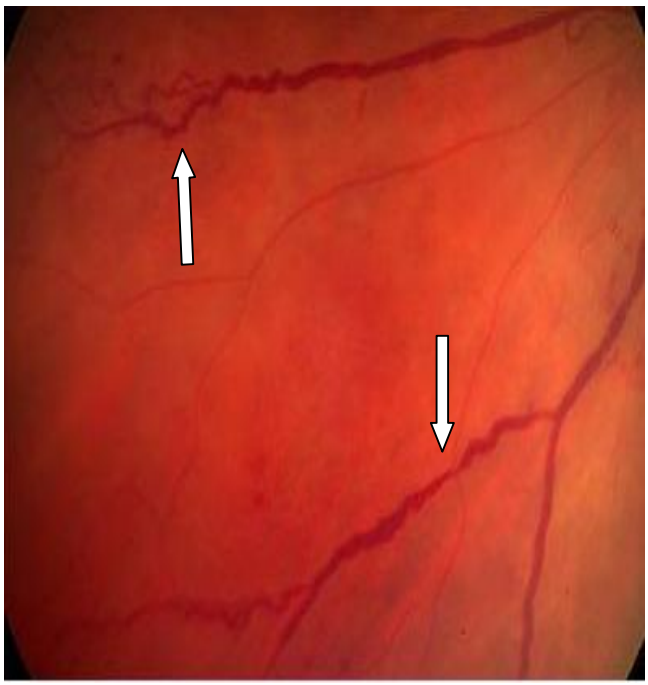
Severe NPDR



PDR

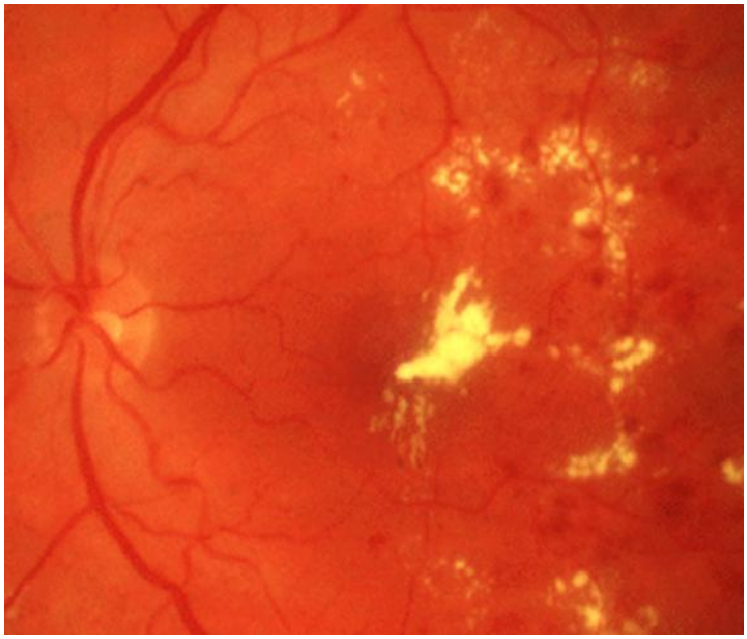


Intra Retinal Microvascular Abnormalities

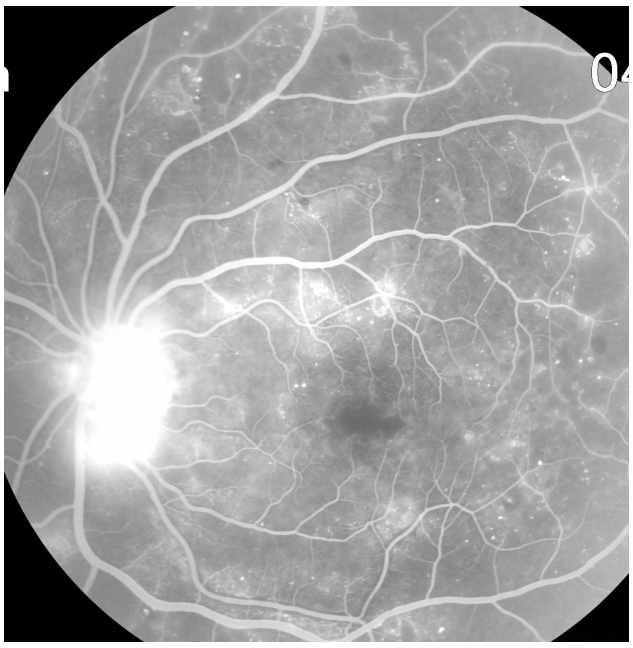


Venous Abnormalities

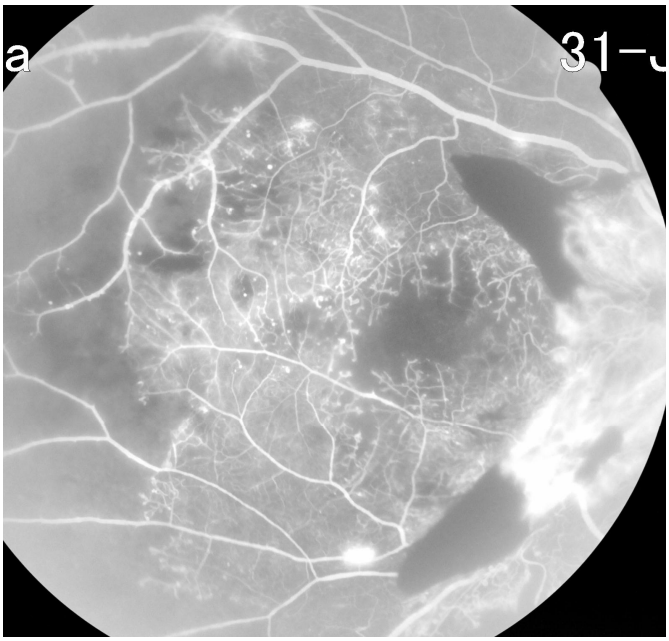
Neovascularisation Elsewhere



Clinically Significant Macular Edema

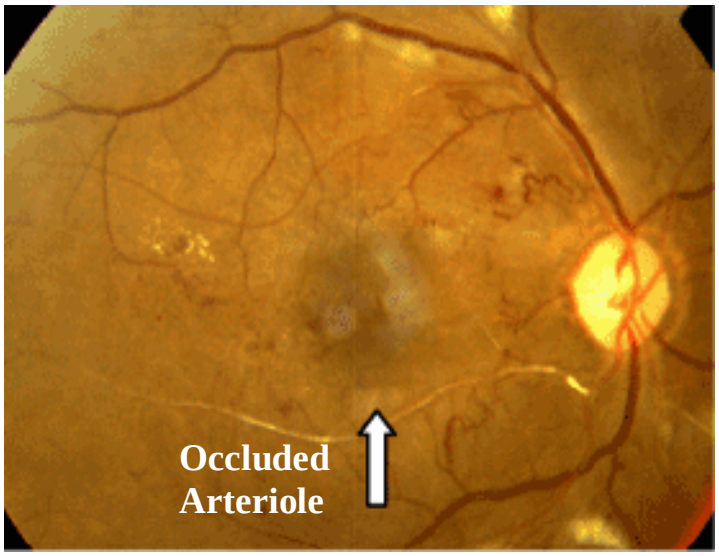


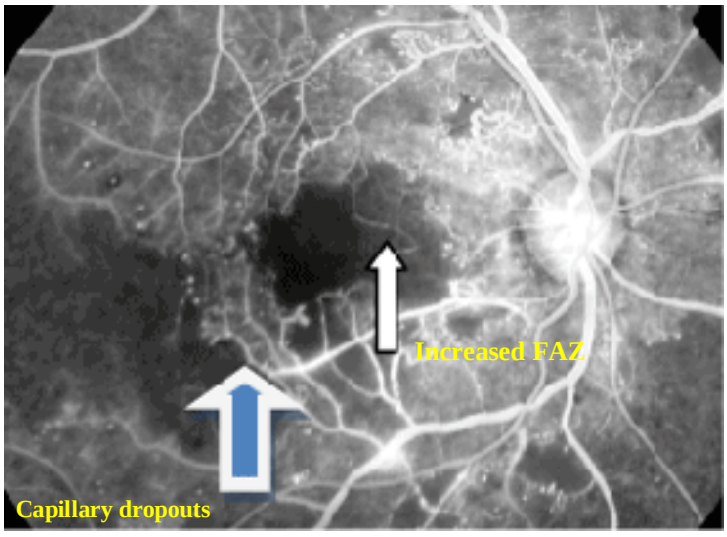
MILD MACULAR ISCHEMIA



MODERATE MACULAR ISCHEMIA

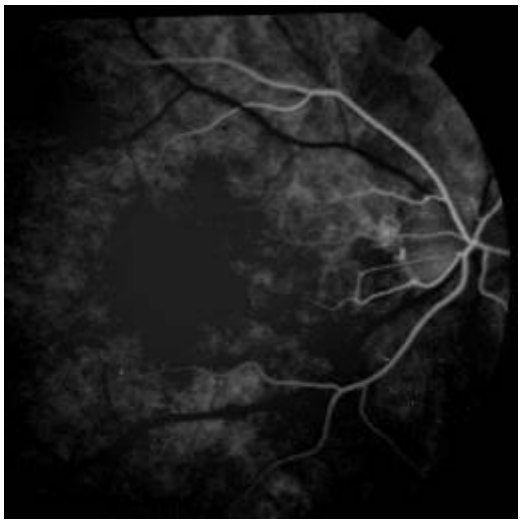
SEVERE MACULAR ISCHEMIA



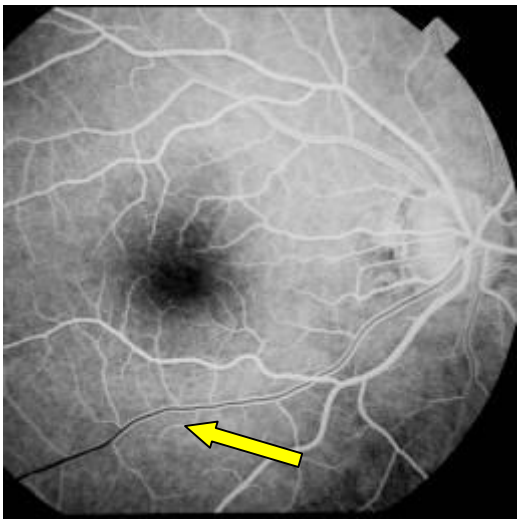


FUNDUS CAMERA

PHASES OF ANGIOGRAM

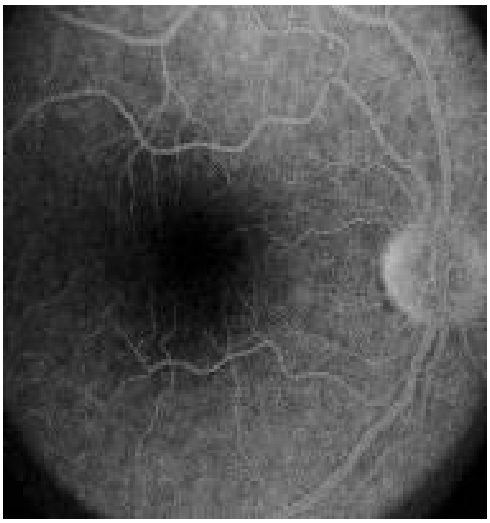


Arterial Phase

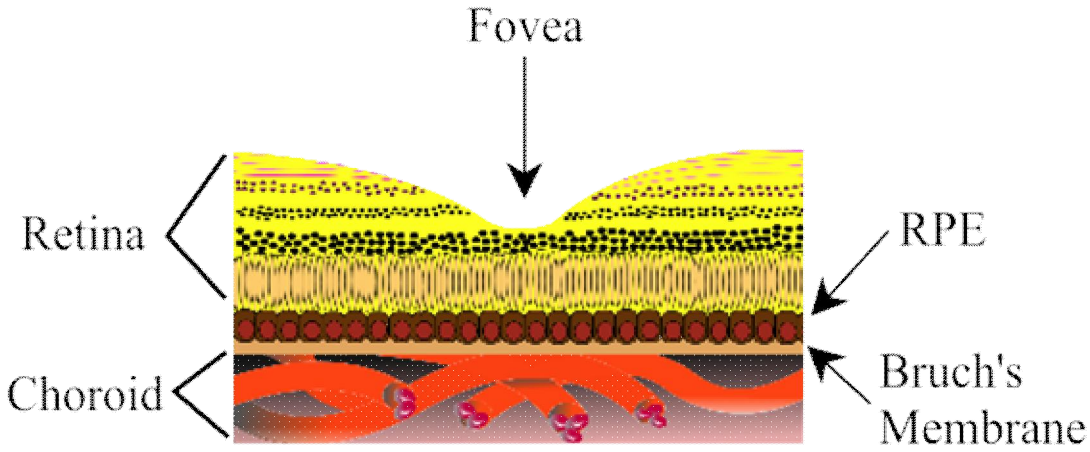


Early Venous Phase Showing Laminar Filling

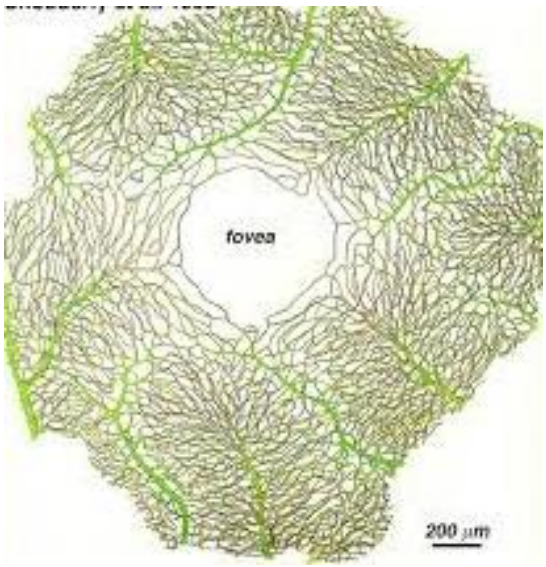
Late Venous Phase



Late Phase

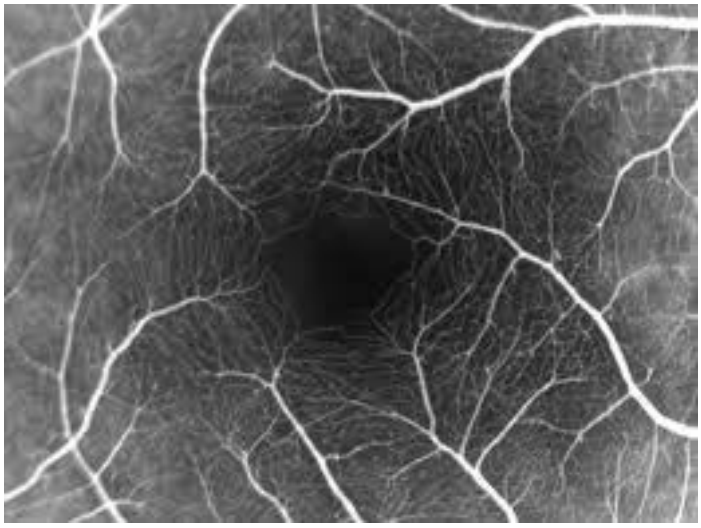


Anatomy of Macula



Perifoveal Capilary Arrangement around the fovea

NORMAL FOVEAL AVASCULAR ZONE (FAZ)



INSTITUTIONAL ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : To determine the association of risk factors in type 2 diabetic patients with diabetic macular Ischemia

Principal Investigator : Dr.M.Kavitha

Designation : PG in MS (Ophthalmology)

Department : Department of Ophthalmology
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 08.04.2013 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

17/9/13

MEMBER SECRETARY,
IEC, SMC, CHENNAI

சுய ஒப்புதல் படிவம்

ஆராய்ச்சி நிலையம் - அரசு ஸ்டான்லி மருத்துவமனை
சென்னை - 600 001.

பங்கு பெறுபவரின் பெயர் -

பங்கு பெறுபவரின் எண் -

பங்கு பெறுபவர் இதனை (✓) குறிக்கவும்.

மேலே குறிப்பிடப்பட்டுள்ள விழியடி இரத்த குழாய் பரிசோதனை ஆய்வு விரவங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாக்களிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நாள் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த பரிசோதனை சம்மந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்கு பெறும், மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்பதற்கு என் அனுமதி தேவையில்லை என அறிந்துகொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக்கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கம் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் அறுவை சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த விழியடி இரத்த குழாய் பரிசோதனை ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப் பட்ட அறிவுரைகளின் படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதி அளிக்கிறேன்.என் உடல் பாதிக்கப்பட்டலோ அல்லது எதிர் பாராத வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணிக்கு தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

ஆய்வாளரின் கையொப்பம். பங்கேற்பவரின் கையொப்பம்.

MASTER CHART

S. No	Name	Age	Sex	Risk factors in yrs				Treatment	Ant.seg findings		BCVA		Fundus		FFA		INV	INV	INV	INV	INV	INV	INV
				DM	HTN	CAD	OTHERS		RE	LE	RE	LE	RE	LE	Macula RE	Macula LE	Bld sugar	HbA1C %	urea	creatinin	lipid pro	urine alb	ECG
1	kandasamy	46	M	15 yrs	-	-	PT 2yrs, CKD	OHA, ATT completed	NAD	NAD	6/24	6/24	PDR	PDR	FAZ-N	FAZ-N	103(F)	6.8	80	2.7	186	2+	WNL
2	senthil	40	M	10 yrs	5yrs	-	It dia foot,CKD	OHA, anti HTN drugs 5th toe amputated	NAD	NAD	6/60	6/60	PDR with CSME	PDR with CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	145(F)	6.1	170	6.7	198	2+	WNL
3	jaithun bee	45	F	13 yrs	-	-	-	OHA	NAD	NAD	6/18	6/18	Sev.NPDR / CSME	Sev.NPDR / CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	226(PP)	6.9	32	1.3	167	1+	WNL
4	Govindaraj	57	M	6 yrs	-	-	-	OHA	NAD	NAD, divergent	6/24	6/18	Sev.NPDR / CSME	Sev.NPDR / CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	428(F)	8.2	18	1	159	trace	WNL
5	Rajaram	45	M	15 yrs	rec. diagno	-	PT 5yrs	OHA, anti HTN drugs, ATT completed	NAD	NAD	6/12	6/24	PDR/maculopathy	PDR	FAZ-N	focal capillary dropout+	233(F)	6.8	32	1	225	trace	WNL
6	kumar krishnan	38	M	6 yrs	5 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/36	6/36	Sev.NPDR / CSME/gr 2 HTN retinopathy	Sev.NPDR / CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	149(PP)	6.5	26	0.8	189	nil	WNL
7	krishna murthy	55	M	5 yrs	6 months	-	-	OHA, anti HTN drugs	IMC	IMC	6/18	6/60	Sev.NPDR / gr 2 HTN retinopathy	Sev.NPDR	FAZ-N	FAZ-N	152(F)	6.2	28	0.7	228	nil	WNL
8	Kursheed banu	53	F	10 yrs	-	2 yrs	-	OHA, anti anginal drugs	IMC	IMC	6/24	6/60	Sev.NPDR / focal CSME	Sev.NPDR / CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	136(F) 259(PP)	6.9	42	0.1	252	nil	changes+
9	Mohan	60	M	9 yrs	-	-	-	OHA	lens changes	IMC	6/18	6/18	Sev.NPDR	Sev.NPDR / CSME	FAZ-N	N, macula leaks+	276(F)	7.1	48	3.8	168	2+	ST Changes+
10	Muniammal	55	F	5 yrs	3 yrs	-	-	OHA, anti HTN drugs	IMC	IMC	6/18	6/60	Mod.NPDR/gr 2 HTN retinopathy	Mod.NPDR/ gr 2 HTN retinopathy	FAZ-N	FAZ-N	234(F)	6.4	24	0.6	152	nil	WNL
11	Kasthuri	60	F	7 yrs	2 yrs	-	-	OHA, anti HTN drugs	IMC	IMC	6/12	6/18	Mod.NPDR/CSME	Mod.NPDR/ CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	116(F)	6.2	34	0.8	174	nil	WNL
12	Anthony	40	F	7 yrs	rec.diagno	-	-	OHA, anti HTN drugs	NAD	NAD	6/12	6/18	Mod.NPDR	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	112(F)	6	27	0.8	224	nil	WNL
13	Pattammal	70	F	10 yrs	3 yrs	-		OHA, anti HTN drugs	PSCC	PSCC	6/12	6/36	Mild NPDR	Mild NPDR/CSME	focal capillary dropout+ / macular leaks	FAZ-N, macula leaks+	166(F)	6.5	32	0.9	196	trace	WNL
14	Meenakshi	57	F	10 yrs	rec.diagno	2 yrs	-	OHA, anti HTN drugs, antianginal drugs	NAD	NAD	6/12	6/12	Mod.NPDR	Mod.NPDR	FAZ-N	FAZ-N	122(F)	5.9	28	0.6	223	nil	changes+
15	Sathya	60	F	20 yrs	-	-	-	OHA	IMC	IMC	HM+	6/24	Sev.NPDR /? Ischaemic maculopathy	Sev.NPDR	FAZ increased	FAZ-N	142(F)	6.4	29	0.9	195	trace	WNL
16	kanakambal	70	F	8 yrs	3 yrs	-	-	OHA, anti HTN drugs	IMC	PC IOL	6/18	6/18	Mild NPDR/ Maculopathy	Mod.NPDR	FAZ-N	FAZ-N	101(F)	6	35	1	175	nil	WNL
17	Prahaladan	55	M	13 yrs	2 months	-	PT 7yrs	OHA, anti HTN drugs, ATT completed	NAD	NAD	6/12	6/36	PDR	PDR with CSME	FAZ-N	FAZ-N, macula leaks+	111(F)	6.7	30	0.5	186	nil	WNL
18	lakshmi	68	F	20 yrs	-	-	-	OHA	PC IOL	PC IOL	6/36	1/60	Sev.NPDR / maculopathy	Sev.NPDR / maculopathy	FAZ increased	FAZ increased	169(F)	7.2	41	0.8	178	trace	WNL
19	Devika	52	F	5 yrs	rec.diagno	3 months	-	Insulin, anti HTN drugs,anti anginal drugs	IMC	IMC	6/12	6/12	Mod.NPDR	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	118(F)	6.2	34	0.6	168	nil	changes+
20	Sakul hameed	48	M	10 yrs	6 yrs	-	-	Insulin, anti HTN drugs	IMC	IMC	6/9	6/9	Mod.NPDR	Mod.NPDR	FAZ-N	FAZ-N	108(F)	5.8	36	0.8	186	nil	WNL
21	Revathi	52	F	10 YRS	10 YRS	3 months	-	OHA, anti HTN drugs, antianginal drugs	Early lens changes+	Early lens changes+	6/9	6/9	Mild NPDR/ Maculopathy	Mod.NPDR	FAZ-N	FAZ-N	119(F)	6	18	0.7	149	nil	changes+
22	govindammal	55	F	5 yrs	rec.diagno	1 yr	-	OHA, anti HTN drugs, antianginal drugs	Early lens changes+	Early lens changes+	6/12	6/9	Mod.NPDR	Mod.NPDR	FAZ-N	FAZ-N	132(F)	6.6	23	1.1	126	nil	changes+

23	Vijaya	49	F	5 yrs	1 yr	-	-	OHA, anti HTN drugs	Early lens changes+	Early lens changes+	6/18	6/12	Sev.NPDR	Sev.NPDR	FAZ-N	FAZ-N	138(F)	7.2	19	0.6	232	nil	WNL
24	Gursheed begum	59	F	10 yrs	-	-		OHA	IMC	IMC	5/60	5/60	Sev.NPDR / CSME	Sev.NPDR / CSME	FAZ increased / macular leaks	FAZ increased / macular leaks	236(F)	7.8	24	0.7	202	trace	WNL
25	Vedanayagam	55	M	20 yrs	1 yr	-	-	OHA, anti HTN drugs	IMC	IMC	6/12	6/12	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N, macula leaks+	FAZ-N, macula leaks+	186(F)	6.5	22	0.5	235	trace	WNL
26	Kamala	65	F	12 yrs	8 yrs	5 yrs	-	OHA, anti HTN drugs, antianginal drugs	IMC	IMC	6/12	6/18	Mod.NPDR	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	119(F)	6.3	39	0.9	196	nil	changes+
27	Vimalan	46	M	10 yrs	2 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/12	6/12	Sev.NPDR	Sev.NPDR	FAZ-N	FAZ-N	138(F)	6.7	32	0.6	248	nil	WNL
28	kandasamy	58	M	10 yrs	-	3 Yrs	-	OHA, antianginal drugs	IMC	IMC	6/12	6/12	Mod.NPDR	Mod.NPDR	FAZ-N	FAZ-N	110(F)	6.1	27	0.8	188	nil	WNL
29	Vasu	46	M	8 yrs	1 yr	-	CKD	OHA, anti HTN drugs	NAD	NAD	6/24	6/24	Sev.NPDR / CSME	Sev.NPDR / CSME	focal capillary dropout+	focal capillary dropout+	132(F)	6.8	83	2.7	250	1+	WNL
30	Mohan	67	M	10 yrs	-	-	CKD	OHA, insulin	lens changes+	lens changes+	6/18	6/18	Sev.NPDR/ maculopathy	Sev.NPDR / CSME	FAZ-N	FAZ-N, macula leaks+	79(F)	6.4	63	3.8	194	2+	changes+
31	Vimala devi	44	F	5 yrs	-	-	-	OHA	NAD	NAD	6/12	6/9	Mod.NPDR	Mod.NPDR	FAZ-N	FAZ-N	119(F)	6.1	12	0.8	189	nil	WNL
32	Pankajavalli	45	F	5 yrs	-	-	-	OHA, insulin	NAD	NAD	6/18	6/18	Mod.NPDR/CSME	Mod.NPDR/ CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	109(F)	6.4	26	0.9	236	nil	WNL
33	lakshmi	60	F	5 yrs	-	-	-	OHA	lens changes+	lens changes+	6/9	6/9	Mild NPDR	Mod. NPDR	FAZ-N	FAZ-N	98(F)	5.8	18	0.6	159	nil	WNL
34	Indrani	60	F	10 yrs	-	-	-	OHA	PC IOL	PC IOL	3/60	6/12	Sev.NPDR / CSME	Mod.NPDR/ maculopathy	FAZ increased/ macular leaks	FAZ-N, macula leaks+	268(F)	7.4	40	1.1	226	trace	WNL
35	lakshmi Sundari	50	F	6 yrs	-	-	-	OHA	NAD	NAD	6/9	6/6	Mod.NPDR/ maculopathy	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	86(F)	5.7	22	0.8	228	nil	WNL
36	Baby	67	F	25 yrs	5 yrs	-	-	OHA, anti HTN drugs	IMC	IMC	6/18	6/18	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N, macula leaks+	FAZ-N, macula leaks+	95(F)	6.3	17	0.8	195	nil	WNL
37	Dasarathan	48	M	5 yrs	5 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/18	6/24	Mod.NPDR/CSME	Mod.NPDR/ CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	296(F)	7.8	20	1.2	205	1+	WNL
38	Sengaiah	56	M	7 yrs	6 months	-	-	OHA, anti HTN drugs	NAD	NAD	6/12	6/9	Mild NPDR/ Maculopathy	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	101(F)	6	17	0.5	198	nil	WNL
39	Ramila	50	F	7 yrs	2 yrs	1 Yr	-	OHA, anti HTN drugs, antianginal drugs	NAD	NAD	6/9	6/9	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N	284(F)	7.2	38	1.1	214	nil	WNL
40	Pakkirisamy	54	M	12 yrs	6 Yrs			OHA, insulin, anti HTN drugs	NAD	NAD	6/18	6/18	Mod.NPDR/CSME	Mod.NPDR/ CSME	focal capillary dropout+ / macular leaks	FAZ-N, macula leaks+	118(F)	6.9	15	0.6	274	nil	WNL
41	Sangeetha	42	F	8 yrs	5 yrs	-	CKD -	OHA, anti HTN drugs	NAD	NAD	3/60	4/60	PDR	PDR	FAZ increased	FAZ increased	189(F)	6.8	58	2.6	183	2+	WNL
42	Basheer	52	M	13 yrs	-	-	-	OHA, insulin	lens changes+	lens changes+	5/60	6/60	PDR/maculopathy	PDR/maculopathy	FAZ-N, macula leaks+	FAZ-N, macula leaks+	227(F)	7.6	19	0.8	128	nil	WNL
43	Raman	67	M	12 yrs	12 Yrs	-	-	OHA, anti HTN drugs	PC IOL	PC IOL	6/9	6/18	Mod.NPDR/ maculopathy	Mod.NPDR/ CSME	FAZ-N	FAZ-N, macula leaks+	132(F)	6.4	60	0.8	208	nil	WNL
44	Mohana	55	F	5 yrs	3 yrs	-	-	OHA, anti HTN drugs	lens changes+	lens changes+	6/24	6/24	Mod.NPDR/CSME	Mod.NPDR/ CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	123(F)	6.8	17	0.5	266	nil	changes+
45	Kuppammal	62	F	15 yrs	10 Yrs	-	-	OHA, anti HTN drugs	IMC	IMC	4/60	6/60	PDR	PDR/ maculopathy	FAZ-N	FAZ increased /Macular leaks	246(F)	7.9	20	0.9	145	trace	WNL
46	Jeyaraj	57	F	7 yrs	7 Yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/12	6/9	Mod.NPDR/CSME	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	237(F)	7.1	38	1.5	187	1+	WNL
47	Anjalai	60	F	6 yrs	1 YR	-	-	OHA, anti HTN drugs	NAD	NAD	6/9	6/9	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N	296(F)	7.5	47	0.9	231	trace	WNL
48	lakshmi	50	F	6 yrs	2 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/36	6/60	Mod.NPDR	PDR	focal capillary dropout+	focal capillary dropout+	286(F)	8.2	36	0.8	145	1+	WNL
49	Alagu meena	55	F	6 yrs	6 yrs	-	-	OHA, anti HTN drugs	IMC	IMC	6/12	6/36	Mild NPDR/ Maculopathy	Sev.NPDR / CSME	Focal cap.drop outs / few macular leaks	FAZ increased / macular leaks	137(F)	6.5	34	0.7	187	trace	WNL
50	Sankar	50	M	12 yrs	-	-	-	OHA	NAD	NAD	6/12	6/36	Mod.NPDR/ maculopathy	V.Sev.NPDR/ maculopathy	focal capillary dropout+	focal capillary dropout+	182(F)	6.7	52	1.3	176	1+	WNL

51	Ganesan	55	M	6 yrs	-	6 Months	-	Insulin,anti anginal drugs	NAD	NAD	6/6	6/6	Mild NPDR	Mild NPDR	FAZ-N	FAZ-N	140(F)	6.2	22	0.7	142	nil	WNL
52	Pushpa	62	F	7 yrs	2 yrs	-	-	OHA, anti HTN drugs	IMC	IMC	6/36	6/36	Mild NPDR/ Maculopathy	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	115(F)	6	18	0.6	185	nil	WNL
53	Parameswari	63	F	15 yrs	10 Yrs	-	thyroid	OHA, anti HTN drugs,	lens changes+	lens changes+	6/6	6/6	Mild NPDR/ Maculopathy	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	96(F)	5.9	21	0.8	167	nil	WNL
54	Nagamma	70	F	8 yrs	-	-	-	OHA	PC IOL	PC IOL	6/12	6/12	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N	310(F)	7.2	23	0.9	237	nil	WNL
55	Indhumathy	48	F	7 yrs	-	-	-	OHA	NAD	NAD	6/9	6/9	Mild NPDR/ Maculopathy	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	121(F)	6.2	22	0.8	145	nil	WNL
56	Mani	65	M	10 yrs		15 yrs	-	OHA, antianginal drugs	PC IOL	PC IOL	6/9	6/9	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N	118(F)	6.3	18	0.7	208	nil	WNL
57	Dhavamani	59	M	14 Yrs	-	-	seizure	OHA, antiepileptics	PC IOL	PC IOL	6/12	6/12	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	focal capillary dropout+	FAZ-N	96(F)	6.3	34	0.9	232	nil	WNL
58	Arul selvi	47	F	5 yrs	6 months	-	-	OHA, anti HTN drugs	NAD	NAD	6/6	6/6	Mod.NPDR/ maculopathy	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	225(F)	7	22	0.6	245	nil	WNL
59	Chandra	55	F	6 yrs	-	-	-	OHA	lens changes+	lens changes+	6/12	6/12	Sev.NPDR / CSME	Sev.NPDR / CSME	focal capillary dropout+ / macular leaks	focal capillary dropout+ / macular leaks	175(F)	6.8	18	0.7	231	nil	WNL
60	Vahit	62	M	5 yrs	-	-	Cirrhosis liver	OHA	Early PSCC	Early PSCC	6/24	6/24	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N	149F)	6.5	16	0.4	245	nil	WNL
61	Amirtha kani	62	F	8 yrs	-	-	-	OHA	NAD	NAD	6/12	6/18	Mild NPDR/ Maculopathy	Mild NPDR/ Maculopathy	FAZ-N	FAN-N	126(F)	5.9	21	0.6	168	nil	WNL
62	Salomi	50	F	6 yrs	1 yr	-	-	OHA, anti HTN drugs	NAD	NAD	6/6	6/6	Mod.NPDR	Mod.NPDR	FAZ-N	FAZ-N	168(F)	7.2	19	0.8	185	nil	WNL
63	Mariyambee	63	F	5 yrs	5 yrs	-	-	OHA, anti HTN drugs	lens changes+	lens changes+	6/9	6/9	Mild NPDR/ Maculopathy	Mild NPDR/ Maculopathy	FAZ-N	FAZ-NN	111(F)	6.2	32	0.6	196	nil	WNL
64	Sunitha	48	F	8 yrs	-	-	-	OHA	NAD	NAD	6/6	6/6	Mod.NPDR	Mod.NPDR	FAZ-N	FAZ-N	146(F)	6.1	26	0.7	239	nil	WNL
65	mani	55	M	7 yrs	4 Yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/9	6/9	Mild NPDR/ Maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N	123(F)	6.4	22	0.6	149	nil	WNL
66	jaya	63	M	8 yrs	8 yrs	2 Yrs	-	OHA, anti HTN drugs, antianginal drugs	lens changes+	lens changes+	6/36	6/24	v.Sev.NPDR/ maculopathy	V.Sev.NPDR/ maculopathy	focal capillary dropout+	FAZ-N, macula leaks+	263(F)	7.8	45	1.3	286	nil	changes+
67	victoria	52	F	7 Yrs	2 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/18	6/12	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	focal capillary dropout+ / macular leaks	FAZ-N, macula leaks+	235(F)	6.8	39	0.6	163	nil	WNL
68	kanagaraj	58	M	11 Yrs	10 Yrs	9 yrs	-	OHA, anti HTN drugs, antianginal drugs	lens changes+	lens changes+	6/12	6/12	Sev.NPDR/ maculopathy	Sev.NPDR/ maculopathy	FAZ-N	FAZ-N	112(F)	6..4	21	0.5	179	trace	changes+
69	Chinnakannu	72	M	21 Yrs	18 yrs	10 yrs	-CKD	OHA, anti HTN drugs, antianginal drugs	PC IOL	PC IOL	6/12	6/9	Mod.NPDR/ maculopathy	Sev.NPDR/ maculopathy	FAZ-N	FAZ-N, macula leaks+	302(F)	8.1	73	2.3	186	1+	changes+
70	nagamma	70	F	13 Yrs	10 Yrs	-	-	OHA, anti HTN drugs	PC IOL	PC IOL	6/12	6/18	Mod.NPDR	Sev.NPDR	focal capillary dropout+ / macular leaks	focal capillary dropout+	310(F)	7.4	34	0.8	286	nil	WNL
71	sarbunisha	52	F	9 yrs	-	-	-	OHA	NAD	NAD	6/9	6/9	Mild NPDR	Mod.NPDR	FAZ-N	FAZ-N	145(F)	6.8	43	0.9	297	nil	WNL
72	Mohan	50	M	6 yrs	8 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/9	6/12	Mild NPDR/ Maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N	218(F)	6.7	34	0.8	178	1+	WNL
73	Syed bee	65	F	15 Yrs	10 yrs	2 yrs	CKD	OHA, anti HTN drugs, antianginal drugs	PC IOL	PC IOL	6/12	2/60	Sev.NPDR	Sev.NPDR/ CSME	FAZ-N	FAZ increased / macular leaks	165(F)	7.6	52	2.1	254	1+	changes+
74	Ravi chandran	56	M	8 Yrs	3 yrs	-	-	OHA, anti HTN drugs	Early PSCC	Early PSCC	6/12	6/18	Sev.NPDR / maculopathy	Sev.NPDR/ CSME	FAZ-N	FAZ-N, macula leaks+	134(F)	6.4	51	1.6	188	trace	changes+
75	Kasiammal	52	F	6 Yrs	6 Yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/18	6/24	Mod.NPDR/ maculopathy	Sev.NPDR / maculopathy	focal capillary dropout+	focal capillary dropout+	121(F)	6.9	34	1	225	trace	WNL
76	Raman	58	M	7 yrs	-	5 yrs	-	OHA, antianginal drugs	NAD	NAD	6/9	6/12	Mod.NPDR/ maculopathy	Sev.NPDR/ CSME	FAZ-N	FAZ-N, macula leaks+	143(F)	6.2	22	0.8	264	nil	changes+

77	faridabanu	60	F	9 Yrs	7 yrs	5 yrs	-	OHA, anti HTN drugs, antianginal drugs	PC IOL	PC IOL	6/12	6/9	Sev.NPDR / maculopathy	Sev.NPDR / maculopathy	focal capillary dropout+	FAZ-N	236(F)	7.5	49	1.8	158	1+	changes+
78	kannaian	54	M	11 Yrs	12 Yrs	-	-	OHA, anti HTN drugs	IMC	IMC	6/24	6/24	Sev.NPDR/ CSME	Sev.NPDR/ CSME	FAZ-N, macula leaks+	FAZ-N, macula leaks+	231(F)	6.6	31	0.7	234	nil	WNL
79	Indhumathy	48	F	7 Yrs	-	-	-	OHA	NAD	NAD	6/9	6/12	PDR/maculopathy	PDR/ maculopathy	FAZ-N	focal capillary dropout+ / few macular leaks+	129(F)	6.7	22	0.8	176	trace	WNL
80	gangadhar	67	M	8 yrs	-	-	-	OHA	IMC	IMC	6/18	6/18	Sev.NPDR / maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N	145(F)	6.1	17	0.5	188	nil	WNL
81	Parameswaran	53	M	11 Yrs	10 yrs	1 yr	-	OHA, anti HTN drugs, antianginal drugs	NAD	NAD	6/18	6/12	Sev.NPDR / maculopathy	Sev.NPDR / maculopathy	focal capillary dropout+ / few macular leaks+	FAZ-N	145(F)	6.3	63	1.1	197	trace	changes+
82	shanthi	63	M	14 Yrs	16 Yrs	-	-	OHA, anti HTN drugs	lens changes+	lens changes+	6/12	6/9	Mod.NPDR	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	122(F)	5.8	21	0.6	174	nil	WNL
83	Kulasekaran	59	M	16 Yrs	16 Yrs	13 Yrs	CKD	OHA, anti HTN drugs, antianginal drugs	IMC	NAD	6/18	6/9	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N, macula leaks+	FAZ-N, macula leaks+	142(F)	6.4	73	1.6	279	trace	WNL
84	Raja	58	M	8 Yrs	10 yrs	-	CKD	OHA, anti HTN drugs	PC IOL	PC IOL	6/12	6/12	V.Sev.NPDR / maculopathy	V.Sev.NPDR / maculopathy	focal capillary dropout+ / few macular leaks+	focal capillary dropout+ / few macular leaks+	228(F)	7.3	72	1.8	243	2+	WNL
85	Mohammed ibrahim	54	M	7 Yrs	4 yrs	6 months	-	OHA, anti HTN drugs, antianginal drugs	lens changes+	lens changes+	6/12	6/12	Sev.NPDR / maculopathy	Mod.NPDR/ maculopathy	focal capillary dropout+	FAZ-N	139(F)	6.1	21	0.6	288	NIL	WNL
86	punithavathy	62	F	12 yrs	-	-	=	OHA	lens changes+	lens changes+	6/12	6/18	V.Sev.NPDR / maculopathy	Sev.NPDR / maculopathy	FAZ-N, macula leaks+	FAZ-N, macula leaks+	162F)	7.5	34	1.1	187	1+	WNL
87	fathima begum	55	F	9 yrs	-	9 yrs	-	OHA, antianginal drugs	lens changes+	lens changes+	6/6	6/9	Mild NPDR/ Maculopathy	Mod.NPDR	FAZ-N	FAZ-N	148(F)	6.4	23	0.8	196	nil	WNL
88	Karuppusamy	51	M	6 yrs	6 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	4/60	6/12	V.Sev.NPDR / maculopathy	Sev.NPDR / maculopathy	FAZ increased	FAZ-N	146(F)	6.8	18	0.5	181	trace	changes+
89	umarappa	48	M	6 yrs	-	-	-	OHA	NAD	NAD	6/6	6/9	Mod.NPDR	Mod.NPDR	FAZ-N	FAZ-N	126(F)	6.4	17	0.6	228	nil	WNL
90	duraisamy	72	M	15 yrs	2 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/9	6/9	Mod.NPDR	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	136(F)	6.1	16	0.4	176	nil	WNL
91	Elangovan	62	M	16 Yrs	11 yrs	-	-	OHA, anti HTN drugs	IMC	IMC	6/18	6/24	PDR/maculopathy	PDR/ maculopathy	focal capillary dropout+ / few macular leaks+	FAZ increased	234(F)	7.3	62	2.2	164	1+	WNL
92	suseela	52	F	8 yrs	-	-	-	OHA	NAD	NAD	6/6	6/6	Mild NPDR/ Maculopathy	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	104(F)	5.9	32	1	178	nil	WNL
93	mariappan	63	M	10 Yrs	12 yrs	8 yrs	-	OHA, anti HTN drugs, antianginal drugs	PC IOL	IMC	6/24	6/18	V.Sev.NPDR / maculopathy	V.Sev.NPDR / maculopathy	focal capillary dropout+ / few macular leaks+	FAZ-N	145(F)	6.3	45	0.9	208	nil	WNL
94	nirmala	55	F	7 yrs	7 Yrs	-	-	OHA, anti HTN drugs	lens changes+	lens changes+	6/9	6/9	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N, macula leaks+	106(F)	6.4	23	0.7	176	nil	WNL
95	muniyandi	49	M	6 Yrs	7 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/9	6/9	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N	focal capillary dropout+ / few macular leaks+	132(F)	6.4	32	1	176	nil	WNL
96	Meera bee	52	F	7 yrs	-	-	-	OHA	NAD	NAD	6/6	6/6	Mod.NPDR	Mild NPDR/ Maculopathy	FAZ-N	FAZ-N	135(F)	6.2	20	0.5	185	nil	WNL
97	Banumathy	55	F	6 yrs	6 Yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/18	6/9	Mod.NPDR/CSME	Mod.NPDR/ maculopathy	FAZ-N, macula leaks+	FAZ-N	141(F)	6.6	24	0.6	236	trace	WNL
98	Mallika	55	F	8 yrs	8 yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/9	6/9	Sev.NPDR / maculopathy	Sev.NPDR / maculopathy	FAZ-N	FAZ-N	128(F)	6.8	26	0.8	148	nil	WNL
99	kamatchi	53	F	12 yrs	12 Yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/12	6/12	Mod.NPDR/ maculopathy	Mod.NPDR/ maculopathy	FAZ-N	FAZ-N, macula leaks+	201(F)	7.3	23	0.7	202	trace	changes+
100	Karuppaiah	61	M	7 yrs	7 Yrs	-	-	OHA, anti HTN drugs	NAD	NAD	6/9	6/12	Mod.NPDR/ maculopathy	Sev.NPDR / maculopathy	FAZ-N	FAZ-N, macula leaks+	123(F)	6.1	22	0.6	239	trace	WNL